UNIVERSITY OF TORONTO
MEDICAL JOURNAL

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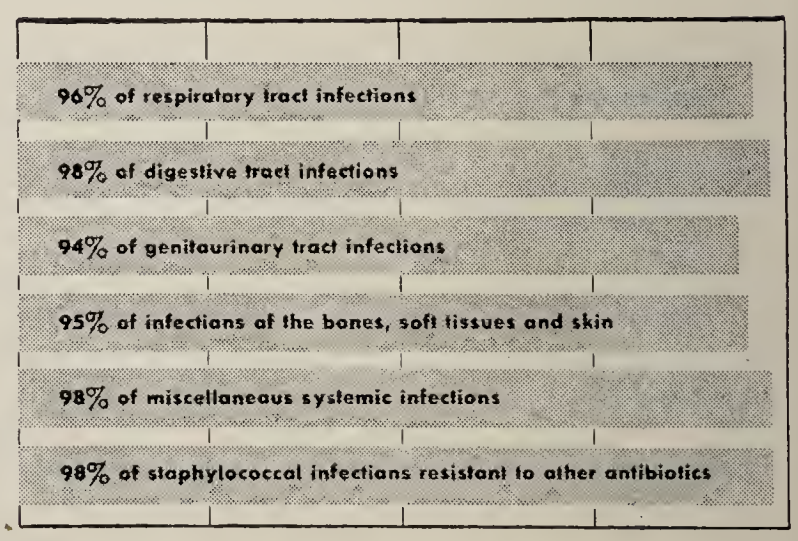
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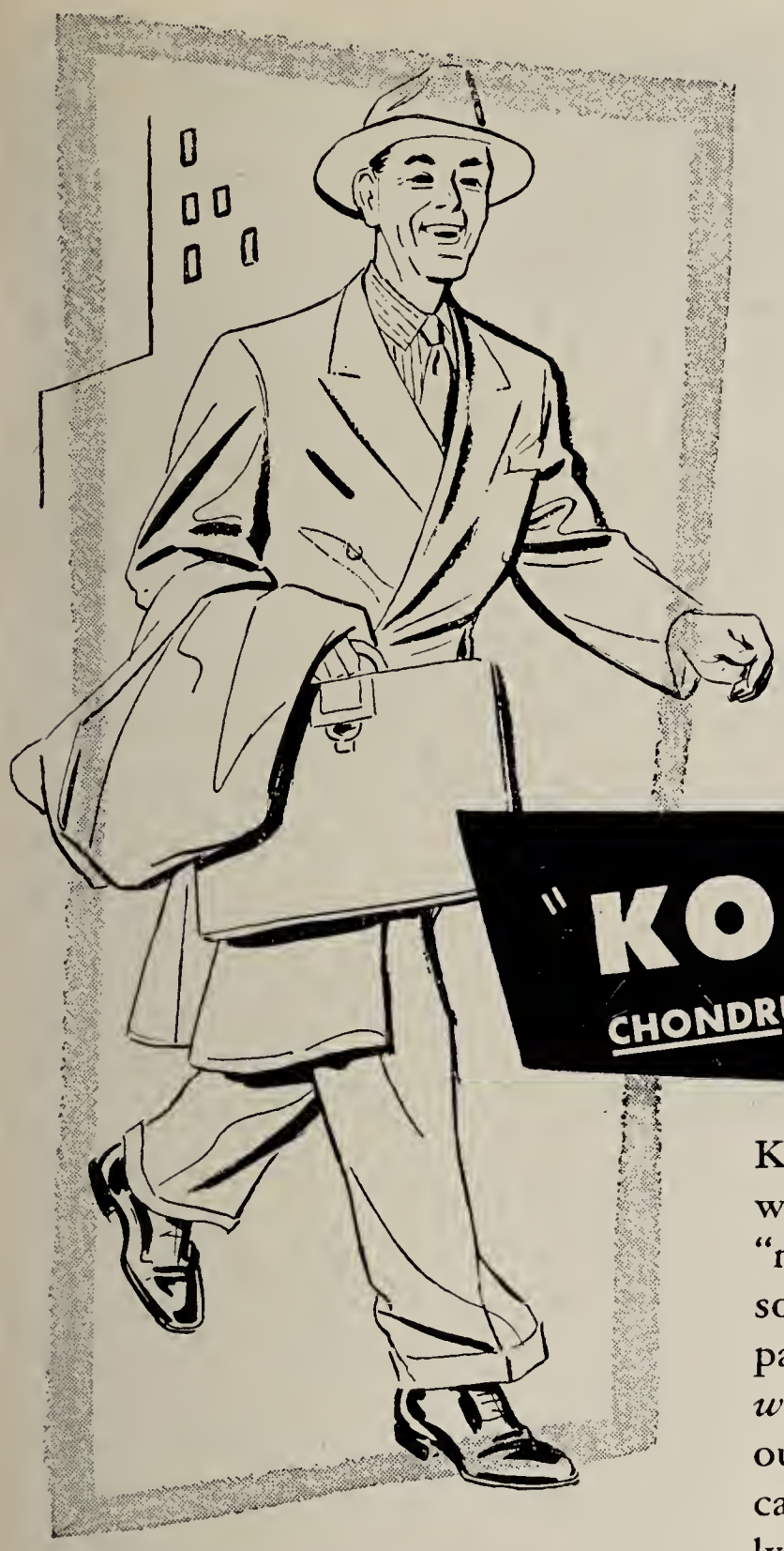

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UNIVERSITY OF TORONTO MEDICAL JOURNAL

ESTABLISHED DECEMBER 1923
AN UNDERGRADUATE PUBLICATION

VOLUME XXXV NUMBER 2
TORONTO, DECEMBER 1957

Editor-in-Chief ..... A. C. Strickler, 5T8

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This Journal is published six times a year from November to April, by the Medical Society of the University of Toronto, to serve primarily as a medium for student expression.

Subscription rates: $3.50 for one volume of six consecutive issues. Single copies 65¢.

Manuscripts including references and footnotes should be typewritten double spaced on one side of the paper. References should be kept to a minimum, and should be cited numerically in the order in which they appear in the text.

Manuscripts in excess of 3,000 words will be considered *unsatisfactory*.

Illustrations are included by arrangement with the Editor. Drawings should be done on white paper in black ink.

Final copy date is the first day of *two months* prior to publication, e.g., September 1 for the November issue.

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Correspondence should be addressed to Room 114, Medical Building, University of Toronto, Toronto 5, Ontario.

Authorized as Second Class Mail, Post Office Department, Ottawa.

PSYCHOLOGICAL ASPECTS OF MATERNAL DEPRIVATION

E. T. BARKER, 5T8

AMONG the most significant developments in psychiatry during the past quarter century has been the steady accumulation of evidence that the quality of parental care which a child receives in his earliest years is of vital importance for his future mental health. More precisely, what is thought to be essential for good mental health is that the infant and young child should experience a warm, intimate, and continuous relationship with his mother (or permanent mother substitute) in which both find satisfaction and enjoyment. The state of affairs in which the child does not have this relationship is termed *maternal deprivation.*

There is much evidence that the deprivation of mother love in early childhood can have far-reaching effects on health. While this paper will deal only with the ill effects suffered by the psyche, it cannot be overstressed that the effects on the soma are every bit as striking! MacLeod of McGill has stated ". . . emotional malnutrition produces the same haggard, withered effect as does its better known brother physical malnutrition. A baby starving for want of affection looks like a baby starving for want of food—and dies just as rapidly."

Evidence of the effects of maternal deprivation falls into three main classes:

a. Direct studies: those by direct observation of the mental health and development of children in institutions, foster homes and hospitals.

b. Retrospective studies: those which investigate the early histories of adolescents or adults who have developed psychological illnesses.

c. Follow-up studies: those which follow up groups of children who have suffered deprivation in their earlier years, with a view to determining their state of mental health.

The extent to which studies of these three types confirm and support each other is impressive. Although there are still far too few systematic studies and statistical comparisons in which proper control groups have been used, when all the evidence is fitted together, it is seen to be remarkably consistent. Undertaken by investigators of varied training, in many countries and in some cases ignorant of each other's conclusions, what each individual piece of work lacks in thoroughness, scientific reliability or precision, is largely made good by the concordance of the whole. Nothing in scientific method carries more weight than this.

Just how we develop as personalities and how this normal development depends on our being in constant touch with some one person who cares for our nourishment and other needs during the critical time of our early years whilst our ability to adjust to the outside world of things and people is growing, is a very interesting question. The following is an oversimplified explanation of the very complex and by no means clearly understood theory which explains the clinical observations of "deprived" children.

To begin with it is thought by most observers that the development of the personality is a process whereby we become less and less at the mercy of our immediate surroundings, and conversely more and more able to choose and create our own surroundings and to plan ahead, often over long periods of time, for the things we want. This necessitates our learning to think in an abstract way,

in order to exercise our imagination, and be able to consider entities other than just our immediate sensations and desires. Only when this "abstract attitude", as it is called, is developed, has the individual the capacity to control his wish of the moment in the interests of his own more fundamental long term needs. One expects, for example, the child of three or even five years to run on to the road to seek his ball, for at those ages he is still largely at the mercy of the immediate situation. As he grows older, however, he is expected to take more things into account and to think ahead. By ten or eleven he is capable of pursuing goals some months distant in time. At sixteen or eighteen the more developed boy or girl is able to perform prodigious feats of abstraction in time and space. It is the development of this "abstract attitude" which is the key to the individual's release from slavery to his urges for immediate satisfaction. To sum up, as the "abstract attitude" develops in the child he is increasingly able to harmonize his different and often conflicting needs: he is able to judge between the things he wants in the future and the things he wants now, he is able to consider what things he desires most, and he is able to realize that some wishes must give way to others. The psychic machinery which we develop within ourselves to harmonize our different and often conflicting needs with the requirements of the world about us is our *ego*. In addition, because one of our foremost long term needs is to remain on friendly and co-operative terms with others, we must keep their requirements firmly in the front of our minds. Indeed, so important is this for us that we differentiate within our ego, machinery specially designed for the purpose—our conscience or *super ego*. The super ego keeps us aware of the things which please and displease the people around us, the things we should or should not do, if we want to live in harmony with others.

It is evident that both the ego and super ego are absolutely dependent for their functioning on our ability to maintain the "abstract attitude". Thus, it is not surprising that during infancy and early childhood when this capacity is not yet developed, the child is unable to act in a thoughtful way with regard to attaining his own ends and to recognizing the claims of others. During this phase of life, the child is, therefore, dependent upon his mother to perform these functions for him. She arranges where he shall be, when he shall eat, sleep, and be washed, and provides for him in every way, allows him to do some things, but checks him in others. She is, in short, his ego and his super ego. Gradually, however, he learns these acts himself, and as he does so, the skilled parent transfers the roles to him in a slow, subtle and continuous progression beginning when he first learns to walk and feed himself, and not ending completely until maturity is reached. Ego and super ego development are thus inextricably bound up with the child's primary human relationships, and it is for this reason that it is thought that only when these relationships are continuous and satisfactory can his personality and conscience develop normally.

Now in dealing here with the embryology of the human mind, one is struck by a similarity with the embryological development of the human body, during the course of which, undifferentiated tissues respond to the influence of chemical organizers. If growth is to proceed smoothly, the tissues must be exposed to the influence of the appropriate organizer at certain critical periods. In the same way, if mental development is to proceed smoothly, it would appear

to be necessary for the undifferentiated psyche to be exposed during certain critical periods to the influence of the psychic organizer—the mother. For this reason, in considering the disorders to which the ego and super ego are liable, it is imperative to have regard to the phases of development of the child's capacity for human relationships. These are many, and naturally, merge into one another. In broad outline the following are most important:

a. the phase during which the infant is in the process of establishing a relation with a clearly identified person—his mother; this is normally achieved by five or six months of age.

b. the phase during which he needs her as an ever present companion; this usually continues until about his third birthday.

c. the phase during which he becomes able to maintain a relationship with her in absentia. During the fourth and fifth years such a relationship can only be maintained in favourable circumstances and for only a few days or weeks at a time; after age seven or eight the relationship can be maintained, though not without strain, for periods of a year or more.

Clinically it is observed that the ego and super ego of children severely deprived in the first phase are not developed, and this is manifested by behaviour that is impulsive and uncontrolled. They are unable to pursue long term goals because they are victims of the momentary whim. For them all wishes are born equal and equally to be acted upon. Their power of checking themselves is absent or feeble, and without this they cannot find their way about the world efficiently.

The case of the child who has a good relation with his mother for a year or two and then suffers deprivation may be rather different. He has passed through the first phase of social development, that of establishing a relationship, and the trauma affects the second phase in which, though ego and super ego development are proceeding apace, the child's awareness of his relative lack of skill in the art of living is reflected in his limpet-like attachment to his mother to whom he constantly looks for help. Only if she is with him or near at hand, can he manage himself and his environment. If he is suddenly removed from her to an institution or hospital, he is faced with tasks which he feels are impossible. He does not understand why he has lost his mother's care; he feels only that he has been deserted.

Now when thinking of the effects of breaking a previously adequate mother-child relationship, it is necessary to remember that a child's restricted sense of time adds greatly to his difficulties. It is exceedingly difficult for grown-ups to remember that the young child's grasp of time is meagre. The child of three can recall only the events of a few days ago, and anticipate those of a day or two hence. Notions such as last week or last month, next week or next month are incomprehensible. Even for a child of five or six, weeks are immensely long, and months almost timeless. This very restricted time span has to be understood if the despair which the young child feels at being left alone in a strange place is to be fully realized. Though to his mother it may seem not only a finite but also a relatively brief time, to him it is eternity. It is this inability to imagine a time of deliverance which, together with the sense of his helplessness, accounts for the overwhelming nature of his anxiety and despair. Perhaps the nearest to it that adults can conceive is to imagine being committed to prison on an indefinite sentence.

Thus, we can see that when a child in

this second phase of development is suddenly removed from his mother, feelings of keen resentment or hostility arise because of his feeling that he has been abandoned. This hostility is variously expressed. It may take the form of tempers and violence; in older children it may be expressed verbally. Those who have treated such children are familiar with the violence of their fantasies against the parents whom they feel have deserted them. Such an attitude is not only incompatible with their desire for love and security, and results in acute conflict, anxiety and depression, but also is clearly inimical to their future social learning. So, far from idolizing their parents and wishing to become like them, one side of them hates them, and wishes to avoid having anything to do with them.

In other cases of deprivation, especially where a child has been shifted during this second phase from one foster home to another, the child has suffered so much pain through making relationships and having them interrupted that he is reluctant ever again to give his heart to anyone for fear of its being broken. It is feelings such as these which underlie the withdrawal response, a response which greatly hampers further development of the personality since progress in human relations requires the capacity to make affectionate relationships, and to identify with loved people.

Deprivation after the age of three or four, namely in the third phase, does not have the same destructive effect on ego and super ego development. Just as the body protects itself from many diseases by a process of immunization, in the same way a child learns to handle the tensions of a normal human existence by exposure to frequent bearable doses of tension early in life. This is, of course, very tricky territory, and no child would ever be removed from his mother intentionally, for the most powerful experience a baby can suffer is separation anxiety. The tensions arising from play with other children provide a much safer technique of immunization.

* * *

Knowledge of the nutritional needs of a child's growing body are now so widespread that orange juice and green vegetables are included in a family's diet as a matter of course. In the new era of medicine just dawning, knowledge of the nurturing of a child's emotions must become equally well accepted. It must be understood that a baby who is fed food alone—is only half fed.

Acknowledgement

The author wishes to express his appreciation to the staff of the Canadian Mental Health Association and the Department of Psychological Medicine, Hospital for Sick Children, Toronto for their helpful suggestions and criticism.

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CONVULSIONS

NORMAN LLOYD, B.A., M.A., 5T8

Introduction, Definition and Classification

FIRSTLY the word seizure as a generic term would be preferable to the term convulsion or fit since this would embrace more logically alterations of pure sensation or consciousness as well as motor manifestations. With this fact in mind the terms convulsion, fit and seizure will be used interchangeably to describe attacks of involuntary tonic or clonic movements of the limbs, trunk, and face with or without loss of consciousness as well as purely sensory attacks.

Although an aetiological classification would be preferable, it is not entirely possible, since the causative agent is often unknown. Similarly a clinical classification would be incomplete because of the "protean" nature of the attacks. Hence, it seems best to classify convulsive disorders largely on an anatomical basis.

A seizure is caused by an abnormal discharge in the cerebral ganglion cells. The discharge which causes the convulsion may be due to the actions on the brain of some local disease or circulating toxin or to an inherent instability of the brain. From an *anatomical* point of view the ganglion cells appear in two areas: (1) the cerebral cortex, and (2) the central gray matter within which is the reticular substance; hence, anatomically one may consider cortical seizures and centrencephalic seizures respectively. In practice some subcortical lesions can be responsible for focal discharge in the cerebral cortex, and this may be called a focal seizure.

From an *aetiological* point of view one may classify fits as (1) idiopathic: those due to an inherent instability of the brain, and (2) symptomatic: those due to local disease or circulating toxin. It seems preferable, however, at this stage to accept the anatomical classification and to add to it two more groups: (1) extra-cerebral seizures due to a general disturbance acting on the brain, viz. hypoglycemia, and (2) a mixed group due to general cerebral disturbance *per se*, viz. cerebral edema and encephalitis.

The working classification will then be:

1. Focal seizures (some subcortical).
2. Centrencephalic seizures.
3. Extra-cerebral seizures.
4. Mixed seizures.

Clinical Aspects

1. focal seizures

Since an abnormal discharge of the ganglion cells may occur in any part of the cerebral cortex and may be either excitatory or inhibitory, it immediately becomes obvious that clinically there may be great variation. The discharge from cerebral ganglion cells may remain localized, in which case a true focal seizure exists, or it may spread over the cortex to produce eventually a generalized seizure. The symptoms caused by the original discharge are referred to as the aura of the seizure, and this provides the most reliable clue to the localization of the underlying disease. In some cases the original discharge may cause no symptoms, and the seizure may appear generalized from the start.

A list of some common focal seizure patterns follows, the diagnosis being made by recognition of the fact that the initial event in the attack is referable to a point in the cortex.

Common Focal Seizure Patterns

CLINICAL TYPE	LOCALIZATION
(1) Somatic Motor	
Jacksonian (local motor)	Pre Rolandic gyrus
Simple adversive	Frontal
(2) Somatic and Special Sensory (auras)	
Somatosensory	Post Rolandic gyrus
Visual	Occipital
Auditory	Temporal
Olfactory	Infratemporal
Gustatory	Sylvian-temporal
(3) Visceral	
Autonomic	Diencephalic
(4) Psychic	
Dreamy state	Temporal
Psychomotor	

As indicated in the above scheme, for example, a discharge arising in the pre Rolandic gyrus would be described clinically as a Jacksonian seizure. This might begin as a twitch in the thumb. A discharge arising in the frontal lobe may cause adversive seizures in which the patient turns his head and eyes away from the side of the lesion.

A discharge arising in the post Rolandic (sensory) cortex will cause abnormal sensations or numbness in the appropriate part of the body. Discharges in the occipital cortex will produce visual disturbances, viz. flashes of light or failure to see in the opposite half field. Discharges in the temporal lobe and some of the adjacent parts of the frontal lobe will produce disturbances of behaviour, viz. psychomotor seizures. These attacks may or may not eventually become generalized.

2. CENTRENCEPHALIC SEIZURES

These arise within the reticular substance (which is probably responsible for the state of consciousness). Due to the widespread connections of the reticular substance, there is a general involvement of the cerebral cortex.

These seizures have been divided clinically into major seizures (grand mal) and minor seizures (petit mal). The *grand mal* is a generalized seizure. In about 50% of the patients there is some type of sensation (aura), which is usually midline, of one part of the body prior to loss of consciousness or the generalized seizure. Typically the aura (which is the first part of the seizure and not a prodrome) is followed by the generalized seizure which begins with a sudden loss of consciousness as the patient enters the tonic phase. This is followed by a clonic phase, exhaustion and finally sleep.

Petit mal seizures may occur alone or in association with grand mal seizures. Clinically there are three types: (1) *simple staring spells* which consist of periods of unconsciousness lasting up to 45 seconds and associated with only minor motor manifestations, viz. eyes turn up, eyelids flicker, and very minor clonic movements of the head; (2) *akinetic seizures* in which there is loss of consciousness and muscle tone; (3) *myoclonic seizures* which consist of sudden jerks of the head or extremities but usually no loss of consciousness. Presumably these three clinical types arise at successively lower levels of the nervous system. The simple staring spells arise at about the level of the thalamus, the akinetic lower down, and the myoclonic seizures at about the

lower brain stem. This, however, is only a rough estimation. The diagnosis of centrencephalic seizures may, therefore, be made if there is an instantaneous loss of consciousness and the attack itself is symmetrical. If an aura occurs, it is midline and not lateralized.

3. EXTRA-CEREBRAL SEIZURES

This group includes those seizures which are the result of a change in the cerebral *environment* and not in the brain itself. The term threshold seizure is sometimes applied to this group since the change in the cerebral environment has to reach a threshold abnormality before a seizure results. Each patient has his own seizure threshold and it is this level which is probably inherited.

In this group may be included hypoglycemia, fever, alkalosis, uremia, toxemia of pregnancy, and anoxia. This is by far the commonest seizure in a child under the age of three years, and may likewise be referred to as a "febrile" convulsion. This can, and usually does, occur in a child who is neurologically normal. The convulsion seems to be the result of a generalized biochemical disturbance. Such seizures are seen rarely in adults except in hypoglycemia. Children, it should be noted, have a low seizure threshold which rises with maturity.

4. MIXED SEIZURES

This group includes seizures which are due to a general cerebral disturbance, i.e. the entire brain is involved. Included here are such entities as cerebral edema and encephalitis. This mixed group might equally well be called a general cerebral disturbance group.

C.N.S. STIMULANTS

It seems appropriate in this discussion of convulsions to consider briefly the central nervous system stimulants. These are roughly classified by their site of action into cerebral, brain stem, spinal and medullary reflex groups. An understanding of the mode of action of these drugs is certainly a step toward understanding the mechanism of convulsions. The explanation would ultimately revolve upon the enzyme systems through which these drugs act in order to reduce synaptic resistance. This is in effect what happens when a drug alters the conditions at the involved synapse by affecting the synchronization of the arriving impulses or reducing the threshold of the post synaptic cell. No general statement can be made with accuracy in our present knowledge. Briefly the empirical evidence shows that the sites of action of drugs producing central nervous system stimulation are:

(1) *Cerebral:* Amphetamine, Methamphetamine, Ephedrine, Atropine, Cocaine, Caffeine.

(2) *Brain stem:* The convulsions seen in this group are clonic in character, consisting of a series of rapidly recurring contractions and relaxations of all muscle groups. These include: Pictrotoxin, Pentylenetetrazol, Nikethamide, Camphor, Menthol, Theophylline and carbon dioxide.

(3) *Spinal:* The spinal cord stimulants cause tonic contractions without a clonic phase. Strychnine is the prototype of this group.

(4) *Medullary reflex:* These drugs act by stimulating the medullary respiratory center reflexly. They have little clinical use in this respect, but include nicotine, cyanides, Apomorphine, and Veratrum alkaloids.

ELECTROENCEPHALOGRAPHY

The electroencephalogram is the most useful single means of investigation of seizures. The test is atraumatic. It consists of applying electrodes to the surface of the scalp and recording the

changes in voltage. These changes are amplified so that an original discharge of 50 microvolts is represented by a 5 millimeter deflection on the ink writing pen. In typical cases the changes in focal seizures and centrencephalic seizures are rather specific. Focal seizures have a focal electroencephalographic abnormality. Centrencephalic seizures have a generalized, and usually bilaterally synchronous, abnormality.

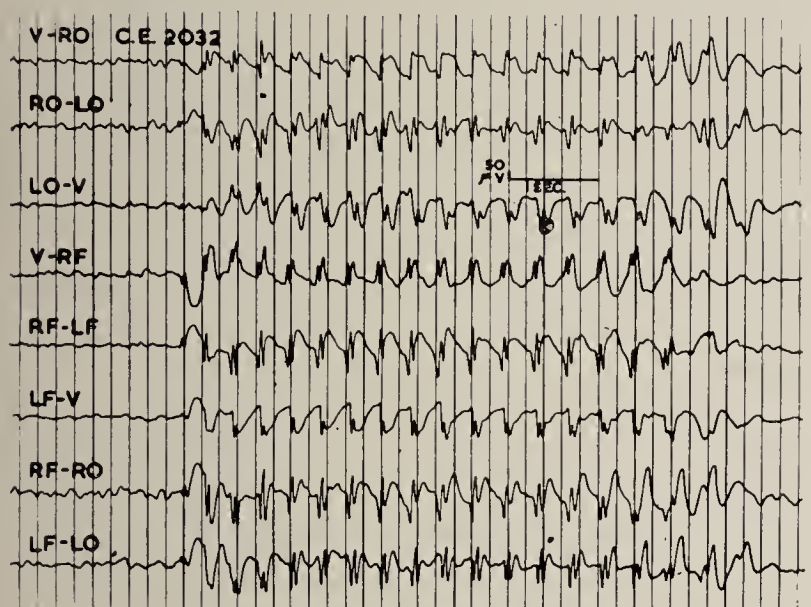

Fig. 1. EEG illustrating centrencephalic seizure.

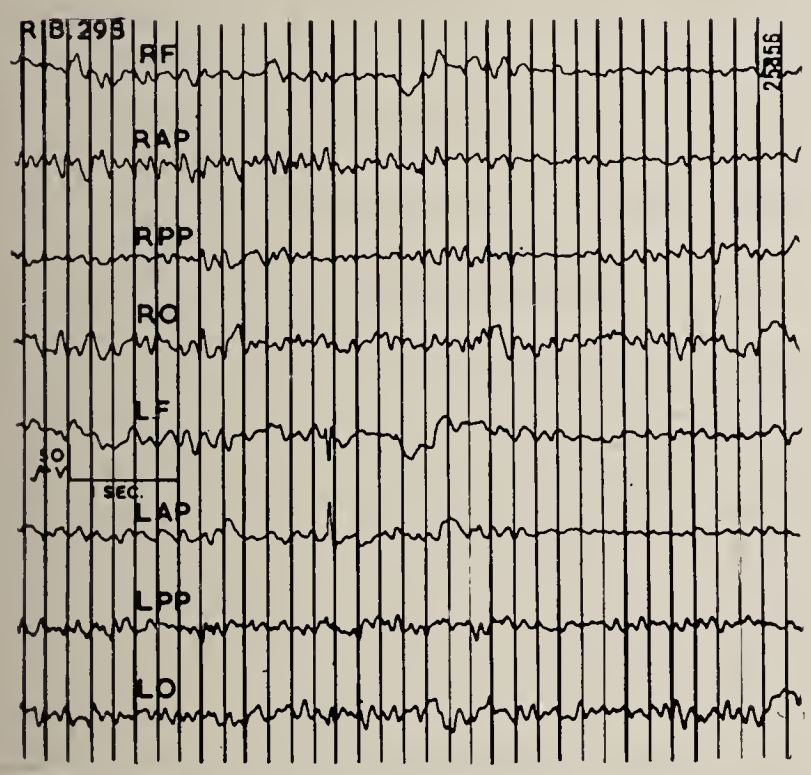

Fig. 2. EEG illustrating focal seizure.

It should be recognized that the frequency of abnormal discharges varies greatly from patient to patient, and every discharge does not produce an overt seizure. In practice it is found that 90% of patients who are liable to recurrent seizures will have at least one subclinical discharge every half-hour. Consequently, it is usual practice to record for at least a one half-hour period. In the 10% of patients who have seizure discharges less frequently than this, longer recording time or repeated examinations may be necessary. It is also advantageous to reproduce as nearly as possible in the electroencephalographic laboratory the conditions under which the patient has his seizures. For instance, if the seizures occur in sleep, then a sedative should be given and the recording should be taken when the patient is asleep.

Patients who have extra-cerebral seizures should have a normal electroencephalogram between seizures, i.e. when the extra-cerebral conditions are not acting to produce a seizure.

Treatment

Since convulsions result from abnormal discharges in the central nervous system, drugs which may be called anticonvulsants are those which have a depressant effect on the central nervous system. All anaesthetic agents and most of the sedatives are capable of suppressing convulsions. Their widespread action on the central nervous system will, however, lead to a simultaneous depression of sensory functions. Of particular importance among anticonvulsant drugs are those which depress motor function and the spreading of abnormal discharges in the central nervous system without marked impairment of the sensorium. Anticonvulsant drugs of this type find their greatest usefulness in the prevention of seizures in the various forms of epilepsy, and may be called antiepileptics.

1. FOCAL SEIZURES

For practical purposes all focal cortical seizures are caused by an organic lesion in the region of the focus. This may be one of many things—tumor, abscess, subdural hematoma, or scar tissue. The treatment is directed primarily at the causative condition. If the cause cannot be removed, then the seizures must be treated symptomatically by anticonvulsant medication. The principle of anticonvulsant therapy is to control the seizure with the smallest possible amount of the least harmful drug. The following types of medication are more generally used: Phenobarbitone, Dilantin, Mysoline, and Mesantoin.

In rare cases a long-standing atrophic cortical focus can be removed surgically. In the best hands 50% of such patients have their seizures completely or almost completely stopped. The indications for surgical excision are: (1) clear evidence of a focal abnormality as the cause of the seizures, and (2) seizures that cannot be adequately controlled in spite of an extensive trial of anticonvulsant medication.

2. CENTRENCEPHALIC SEIZURES

As noted above, these seizures result from discharge occurring in the brain stem or thalamic region, and show no evidence of cortical origin. *Grand mal* or generalized seizures are controlled with the same anticonvulsant medication as that used for the control of the focal cortical seizures. Surgery has no part in the treatment of grand mal seizures.

Tridione is the drug most likely to be of value in *petit mal* seizures. Phenobarbitone may reduce the frequency of attacks, but rarely stops them completely. It is particularly useful in the hyperactive patient. Amphetamine sulfate reduces the number of attacks in some cases. It is generally more useful in the obese, lethargic patient. Milontin is usually less effective than Tridione but is also less toxic. Diamox has been used in petit mal seizures. It is likely to be effective when the attacks can easily be induced by hyperventilation. Initially it has a diuretic action, and it produces a mild acidosis. Ketogenic diets have also been employed.

3. EXTRA-CEREBRAL AND MIXED SEIZURES

These will be considered together with particular reference to the child.

The majority of convulsions stop spontaneously in less than 20 minutes. If they last longer, they should be considered as a medical emergency because there is some evidence that these attacks, particularly if associated with hyperpyrexia, can produce death or irreversible cerebral changes that may be very severe. The most convenient way of stopping an attack is by giving a light ether anaesthetic, using the open mask method. Oxygen if available should be given as well. It is important to keep a clear airway. If the seizure recurs when the anaesthetic wears off, or if vomiting occurs, or if it is difficult to keep a good airway with a mask in place, then paraldehyde intramuscularly is the drug of choice. It has a low toxicity, and it does not depress the respiratory center to any appreciable degree. Intramuscular sodium phenobarbitone may be given instead of paraldehyde. By means of alcohol sponges and fans the child's temperature should be reduced to 101° F. or lower. The child's general disease must be treated. Fluid or electrolyte imbalance must be corrected as soon as possible.

If after 40 minutes of adequate anticonvulsant treatment along these lines the seizure still continues, then more active steps must be taken. For intravenous anticonvulsant therapy, Paraldehyde is the drug of choice because,

unlike the barbiturates, it has very little depressant action on the respiratory center. This is given until the seizure ceases, after which an I.V. drip is set up at such a rate that the seizure is kept just under control.

Where cerebral edema is present, a rapid intravenous injection of 50% glucose solution should be given.

Aspiration of stomach contents occurs readily, and if possible the stomach should be lavaged. A close watch should be kept for evidence of bronchial obstruction, and bronchoscopy may be necessary.

It goes without saying that the most important aspect of the treatment in general is the overall management and psychological assessment of the patient.

ACKNOWLEDGEMENT

The author most gratefully acknowledges the assistance of Dr. J. S. Prichard in the preparation of this article.

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TRANQUILLIZERS—A PROGRESS REPORT

J. B. HOUPT, 5T8

INTRODUCTION

"WE must recollect that all our provisional ideas in psychology will some day be based on an organic substructure. This makes it possible that special substances and special chemical processes . . . provide for the continuation of the individual life in the species (and) we take this probability into account when we substitute special forces in the mind for special chemical substances."[1]

The pendulum that swung many times before Freud taught this in 1914 has swung many times since: from the use of black Hellebore in Ancient Greece, through the "moral treatment" of Pinel, the bloodletting of Benjamin Rush, the era of "focal infection", the use of prolonged sleep, the vogue of the bromides in the middle nineteenth century, the barbiturates—through to the physical and psychotherapies of the twentieth century. We are now climbing to a "virgin field pregnant with possibilities" —the use of the tranquillizers or, as Fahing has called them, ataraxic drugs.

At the time of writing there are more than two dozen tranquillizers or combinations available. In view of this I shall restrict my remarks to four broad chemical groups.

CLASSIFICATION

1. Rauwolfia group, characterized by reserpine.

2. Phenothiazine group:
   chlorpromazine (Largactil, Thorazine)
   mepazine (Pacatal)
   promethazine (Phenergan)
   pyrathiazine (Pyrrolozote)
   promazine (Sparine)
   procloperazine (Compazine)
   ethopropazine (Parsidol)
   diethazine (Dipaicol)

Included here are some compounds which are used as antihistaminics or as drugs for treating Parkinsonism.

3. Benzhydrol group:
   azacyclonol (Frenquel)
   benactyzine (Suavitil)
   hydroxazine (Atarax)

Closely related compounds are the antispasmodic adiphenine (Trasentin), the antiemetic meclizine (Bonamide), and the antihistaminic chlorcyclyzine (Perazil).

4. Substituted propanediols:
   meprobamate (Miltown, Equanil)
   mephenesin (Tolserol, Mephate)

By comparing the physiological and pharmacological actions of these drugs, one can divide them into two broader categories: the *autonomic suppressants* (reserpine, phenothiazine, benzydrol groups) which antagonize the autonomic system regulators acetylcholine, histamine and serotonin; and the *central relaxants* (substituted propanediols) which block hyperexcitable multineuronal reflexes, and relax spastic muscles.[2]

Autonomic Suppressants

1. Rauwolfia

For many centuries the Rauwolfia root was sold in the bazaars of India and advocated for as diverse conditions as pre-eclampsia, snake-bite, hypertension and mania. It was not until Vokil and then Wilkins in 1953 reported the success of the root in the treatment of hypertension, and Hakim in India reported the successful handling of schizophrenia with this drug, that these "new" forms of therapy were considered here. In February 1954, when the first results were reported to the New York Academy of Sciences, the plant was a botanical rarity in the Western world; today more than twenty-five million dollars' worth of Rauwolfia or its derivatives are sold on this continent annually.

To date the results of animal and clinical studies are inconclusive as to the sites or mechanisms of action of Reserpine. They suggest, however, that it acts to diminish afferent impulses from subcortical thalamic centers to the paleocortex or hippocampus and that the calming and sedative effect is due to this alteration in sympathetic-parasympathetic balance by partial suppression of sympathetic activity on the hypothalamus. Areas other than the hypothalamus are apparently affected as evidenced by the extrapyramidal signs and observations that the behavioural effects of ablation of the amygdaloid complex in monkeys are indistinguishable from those produced in a normal animal on reserpine.[3, 4] It is postulated that reserpine acts as a competing antimetabolite for serotonin which may be a central neurohumoral mediator as acetylcholine is in peripheral autonomic ganglia and neuromuscular junctions. Serotonin is present in highest concentrations in the brainstem and in particular the hypothalamus.[5]

PSYCHOSES

With all the ataraxics, the dosage schedule must be individualized; however, in order to realize the full potential of reserpine, it must not be discontinued if the patient becomes agitated in the early stages. Barsa and Kline describe three stages through which the patient may pass:[6]

1. A "sedative" period of 3–10 days during which time the patient becomes less disturbed, easier to manage and perhaps drowsy.
2. A "turbulent" phase of 1 or 2 days up to 3 weeks in which psychotic behaviour may exacerbate, and symptoms of increasing tension and anxiety are prominent. Until this phase is complete, oral or intramuscular therapy must not be discontinued or reduced.
3. The "integrative" period in which he becomes more friendly and interested in his environment. This period lasts from 1 month to an indefinite period.

Not all patients, however, pass through these stages. Some never progress beyond the sedative phase or "if they pass into the turbulent period are unable to achieve enough ego strength to attain the integrative period, and they return to the sedative stage. In such cases, the maximum therapeutic effect is one of sedation."[6] Many of the reported failures in psychoses may be attributed to inadequate dosages or courses of therapy.

The following regimen has been used successfully by Kline. On admission, acutely psychotic patients receive 3 mgm. orally and 10 mgm. intramuscularly (5 mgm. if they are of geriatric age). A minimum of six weeks of combined high parenteral and oral therapy should be undertaken, unless contraindicated by complications or beneficial therapeutic response. If there is no improvement at the end of six months, the drugs may be withdrawn for one or two months and a second course of therapy instituted, following which, improvement may be forthcoming. An oral maintenance dose of 2–3 mgm. once a day is suggested.[4]

Although for schizophrenia the degree of effectiveness has been reported as between 5% and 90% depending on the investigator, the type of schizophrenia treated and the dosage regimen, it is generally agreed that the greater the degree of motor activity and agitation the better the prognosis. In less agitated persons, improvement may appear after the drug has been withdrawn. The shorter the time of hospitalization, the more favourable have been the results, although many chronic psychotics have shown improvement after receiving the drug for as long as two years. Marked improvement in the ward behaviour of most patients has been shown, even if the underlying schizophrenic thought processes persist.[4]

The same dosage regimen may be used with the manic-depressive psychoses as with the schizophrenic; however, due to the property of inducing depression, the drug should be used only on selected cases. With involutional depression ECT is still the indicated form of treatment although some have claimed that remissions have been more lasting with concomitant or maintenance doses of reserpine. The organic psychoses have not responded as well, and indeed patients have a tendency to develop undesirable neurological side effects. The initial parenteral doses should be small and the total should not exceed 5 mgm. Some cases of Huntington's chorea have benefited after high (20 mgm.) parenteral doses.

NEUROSES

There is great diversity of opinion with respect to the use of Rauwolfia alkaloids in the treatment of neuroses. Because of the great number of variables, including the high response of neurotics to placebos and the therapeutic lag of reserpine, the evaluation of these drugs is very difficult. In selected cases of anxiety states it may prove beneficial, perhaps by its pharmacological effect of inducing bradycardia, thereby alleviating palpitation. With these people an initial dose of 0.5 mgm. daily, increasing or decreasing with therapeutic response to as high as 5 mgm. or as low as 0.1 mgm. a day may be effective. Although response may be rapid, the patient should be warned that the action of the drug is slow, and a trial of several weeks should be given before changing the dose. The duration of therapy must also be individualized; it may be discontinued after three to six months or maintained indefinitely.

OTHER USES

The literature is full of reports of

enterprising physicians who have used the tranquillizers "successfully" for a multitude of unrelated syndromes. Because there is no agreement as to the efficacy of these drugs in these conditions, they shall be only briefly mentioned.

Good results have been obtained in Huntington's and Sydenham's chorea. Small doses may be beneficial in epileptics, but prolonged doses may induce convulsions in epileptics and non-epileptics. Parkinsonism may be helped with small (0.1–0.25 mgm.) doses as an adjunct to the usual therapy, but larger doses may make the condition worse. In drug and alcohol addiction, reserpine has proven useful in reducing symptoms and making addicts more amenable to psychotherapy during the withdrawal period; but by itself the drug will not prevent recurrence of the addiction. It should not be used while the patient is in the drug or alcoholic stupor as it may potentiate undesirable reactions. Neurodermatitides have responded very well, due of course to the psychological response rather than any direct specific action. It has also been found useful in tension and hypertensive headaches, infant hyperirritability, enuresis, stuttering and anorexia nervosa.

COMPLICATIONS AND SIDE EFFECTS

Reserpine depressions have been noted frequently especially in hypertensives; this should constitute a warning against the indiscriminate use of this drug in those with tendencies to depression and suicide. If they occur, they usually respond to stimulants or withdrawal of medication with concomitant ECT.

Overdosage with reserpine may yield a syndrome of "reduced appetite after an earlier increase, organic type confusion, and visual hallucinations, either singly or in combination."[4] Reduction of dosage is usually all that is required.

Side effects include: flushing, cramps, diarrhoea and nausea, dizziness, polyphagia, blurring of vision, impotence, lactation, menstrual irregularities and convulsions. These are usually self limited, and do not require treatment.

The psychomotor stimulants such as Dexedrine and Ritalin have been found useful in hypotension, drowsiness, lethargy, fatigue, depression and anorexia. Generalized tremulousness, extrapyramidal symptoms, "turbulence", and insomnia may be treated with mild sedatives.

Other symptomatic therapies include: antihistaminics for facial oedema or seborrheic dermatitis; anticholinergics for ptyalism, muscular cramps, twitching, paraesthesiae and urinary frequency; nasal decongestants for nasal stuffiness.

The drug may have to be withdrawn because of severe disorders of the central nervous system such as hyperpyrexia, ocular palsies and decerebrate movements. It should be noted that a decreased resistance to intercurrent disease has been found clinically and trophic ulcers, diabetic crises, and cardiovascular collapse occur more frequently and more rapidly in reserpine treated patients.

2. Chlorpromazine

Chlorpromazine, an amine derivative of phenothiazine, was developed in France in 1950. Since 1953 it has been widely used for the palliative management of terminal malignancies, in the treatment of narcotic and alcohol habituation, for the control of pain and postoperative nausea and vomiting, and in psychiatric practice.

As with reserpine, experimental and clinical data are inconclusive as to the site(s) and mode of action of chlorpromazine. They suggest that it acts on the hypothalamus, on various components of the reticular activating system, and

that it also has a peripheral autonomic effect. The depression of the hypothalamus, either directly or via depression of the activating system, is thought to alleviate anxiety which is linked with stimulation of hypothalamic areas.[7, 8]

DOSAGE

"If you tell a European that in America we use doses running up to 2–3 Gm. daily, he will throw up his arms and say 'You Americans! In America everything is big—you have big skyscrapers and big automobiles, and it is the same thing with chlorpromazine.' It is interesting to note that the dose changes as one moves from country to country in Europe, and changes with the culture. The English with their calm, placid manner use the lowest dose of 150–300 mgm. daily."[9]

To control acute states of agitation and psychomotor activity, whether the symptoms are manifestations of schizophrenia, manic-depressive, involutional, senile, or toxic psychoses the following therapeutic regimen is suggested. Initially 25 mgm. are given, slowly and deeply intramuscular, repeated in an hour and gradually increased to 100 mgm. every 4 hours if necessary. The patient may become lethargic and sleep for a day or so, but can easily be aroused. Oral doses should gradually replace parenteral doses, increasing until the psychiatric symptoms are controlled (usually around 400 mgm. a day), or until signs of toxicity appear. When the patient has become manageable, psychotherapy may be instituted and the level of chlorpromazine gradually reduced. Improvement has been noted by some after a sudden lowering of dosage. Current evidence is inconclusive, but "the retention of a good remission may require permanent chlorpromazine administration, analagous to the treatment of diabetes or pernicious anaemia".[9] Many workers use a maintenance dose of 75–300 mgm. daily.

PSYCHOSES

There is convincing evidence that chlorpromazine or "pharmacological lobotomy" is the treatment of choice in certain cases of schizophrenia. With intensive drug treatment followed by long-term maintenance, about 80% of acute cases may have sufficient relief of symptoms to permit discharge on convalescent care. About 50% of chronic patients may be permitted to return home although about 25% of these have been found to relapse. These may be due to the chronic relapsing nature of schizophrenia, as well as insufficient psychotherapeutic and family support. Attacks of mania usually subside promptly although relapses are not infrequent. Depressions are often aggravated by the drug, but if accompanied by agitation, they may respond well, especially when the drug is used in conjunction with ECT. Senile and arteriosclerotic agitation and delusional reactions respond well; behaviour is improved and mental confusion reduced without clouding the mental processes. Acute states of panic, postoperative psychoses, toxic and traumatic delirious states regardless of etiology respond very well and the use of chlorpromazine may eliminate the need for physical restraints.[10] Chlorpromazine has also been shown to reduce the hyperactivity and anxiety which had previously prevented mentally defective children from functioning at their true level of ability.[11]

NEUROSES

Like reserpine, there is no specific effect of chlorpromazine in the treatment of the neuroses although it may prove useful where symptoms of tension and anxiety predominate. These may be controlled with 25 mgm. three times a day which can be increased to the

tolerance limit. Hysterical and obsessive-compulsive neuroses, hypochondriases and chronic psychosomatic illnesses have not responded favourably.

OTHER USES

By controlling apprehension, anxiety and restlessness beneficial results have been reported in such varied conditions as physical and psychic pain, arthritis, severe asthma, tension headaches, neurodermatitides, tuberculosis, severe refractory hiccoughs, causalgia, choreas, spastic states, intestinal disorders and acute emotional outbursts associated with epilepsy. The same precautions must be taken with the epilepsies and chlorpromazine as with reserpine. Drug and disease induced nausea and vomiting as well as that associated with pregnancy, irradiation, surgery and paediatric problems have responded very favourably. Chlorpromazine has yielded excellent results in the management of psychomotor agitation and delirium tremens, and minimizes the withdrawal symptoms of alcohol and drug addiction. It aids in making chronic alcoholics more receptive to psychotherapy.

COMPLICATIONS AND SIDE EFFECTS

Jaundice is of the intrahepatic obstructive type. There is blocking of the biliary canaliculi with "biliary thrombi", neutrophilic and eosinophilic infiltration and intact parenchymal cells. Alkaline phosphatase and serum bilirubin are elevated. Stools are acholic. The development of icterus is not related to dosage or previous liver disease, and cannot be predicted by routine liver function tests. It usually occurs after 7 to 20 days of therapy, and lasts about a week, but may last for months. The incidence varies from 0.1% to 4%.[12, 13]

Agranulocytosis has been reported sporadically, but its frequency (less than 0.3%) is not surprising when the amount of drug taken is realized.[14] With chloromycetin, the sulphonamides, and thiouracil therapies, it is useless to do routine white blood counts to forestall this complication unless, of course, infection is present. Rarely have there been serious consequences if the drug is withdrawn and the appropriate measures taken. A few deaths, however, have been reported.

A self-limited dermatitis in the form of a fine macular or maculopapular rash and pruritis which respond well to antihistaminics have been reported. Angioneurotic edema may be associated. Because of reports of photo-sensitivity, it has been suggested that patients on chlorpromazine avoid undue exposure to the sun.

Extrapyramidal symptoms closely resembling Parkinsonism have been noted in those patients on high doses or on long-term therapy. It may be controlled by reducing the dose or by the concomitant use of drugs specific for Parkinsonism.

Chlorpromazine potentiates the action of agents such as barbiturates, narcotics and anaesthetics; about one-quarter to one-half the usual dose of these agents will suffice. The amount of barbiturate used as an anticonvulsant, however, should not be reduced. Alcoholics should be closely supervised if given chlorpromazine as it may potentiate the depressant effects of the alcohol. The antiemetic action of chlorpromazine may mask the signs of drug toxicity, brain tumor or intestinal obstruction.

Postural hypotension may occur with initial parenteral administration and, therefore, the drug should be used with caution in patients with cardiovascular disease or atherosclerosis. It may be controlled by placing the patient in the shock position or administering Levophed. Ephedrine is contraindicated here as its action may be reversed causing a further fall in blood pressure.

Other mild side effects include drowsiness, mouth dryness, nasal congestion, constipation, blurring of vision, fever, increased appetite and weight gain, insomnia, menstrual irregularities and lactation.

Combined Ataraxic and ECT-Ataraxic Therapy

Some workers have reported the increased therapeutic response with combined reserpine-chlorpromazine therapy, but the advantages are slight and the statistics unconvincing. There is no uniformity of opinion on the safety of combined ECT with chlorpromazine or reserpine, but inasmuch as some fatalities have occurred, it is advisable not to use the combination unless there are strong therapeutic indications.[4]

3. Benzhydrol Group

It is claimed that these drugs control acute confusion and hallucinatory states. Since there are many conflicting and contradictory reports in the literature, they will not be elaborated upon. The consensus of opinion is that they have not proven as clinically successful as they have on experimentally induced LSD-25 and mescaline psychoses.

Conclusions

It is difficult to say in which conditions any specific drug is indicated; it seems to depend on the clinician's experience and personal preference. Chlorpromazine appears to be outstandingly superior to other agents with respect to general therapeutic efficiency; however, the extensive use of reserpine is a strong testimonial to its efficacy.

Summary

A review of the history and pharmacology of the tranquillizing drugs has been presented. The modes of action, dosage, indications and complications of reserpine and chlorpromazine have been considered. The benzhydrol group of drugs has been briefly mentioned. The substituted propanediols, characterized by Miltown will be reviewed in a subsequent paper.

Acknowledgement

The author wishes to acknowledge the assistance of Dr. W. B. Spaulding in criticizing and editing this paper.

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FIGURE 1. This middle-aged man noticed increasing difficulty in walking, and began to bump and injure his legs without pain. Name the joint lesion. What is the gross pathology? In what generalized diseases do you see this lesion?

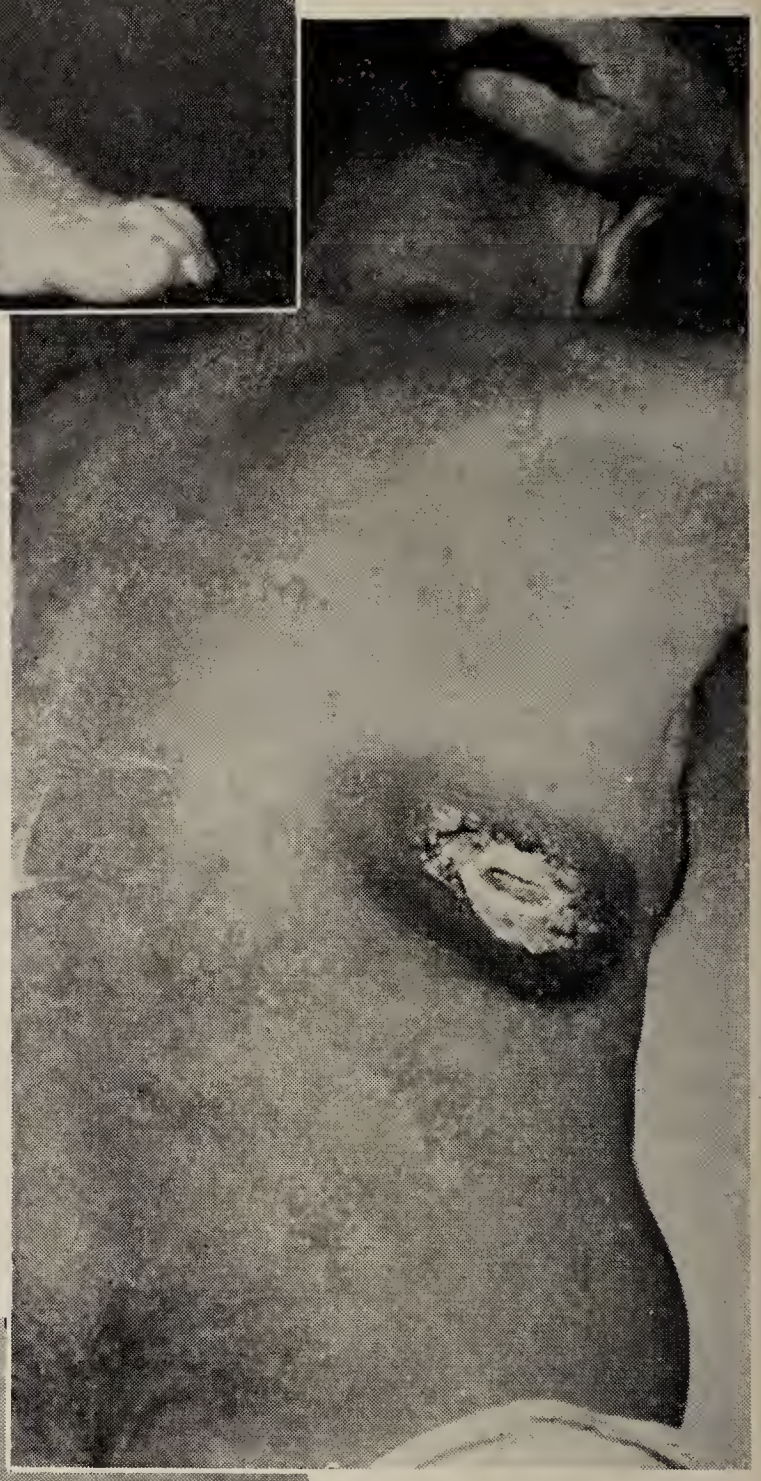

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FIGURE 2. The diagnosis is obvious, isn't it? How would you investigate and treat this lesion?

Careful observation often makes a diagnosis without the physician laying a hand or an instrument upon his patient. Here are six photographs to test your powers of observation. Each has enough clues for you to make the diagnosis. If you can come to some conclusion about the photograph before reading the questions, all the better, as some of them tend to be leading.

You will find the answers on page 76.

←
FIGURE 3. What is the sign illustrated? What is its significance? Outline the underlying physiology. In what clinical conditions can it be elicited?

→

FIGURE 4. This newborn infant was believed to be perfectly normal until its first feeding. Name the lesion. What is the treatment?

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FIGURE 5. Name the condition. Where is the primary pathology? What are the other likely physical findings in the abdomen? Outline the underlying pathophysiology. What simple procedure confirms the diagnosis?

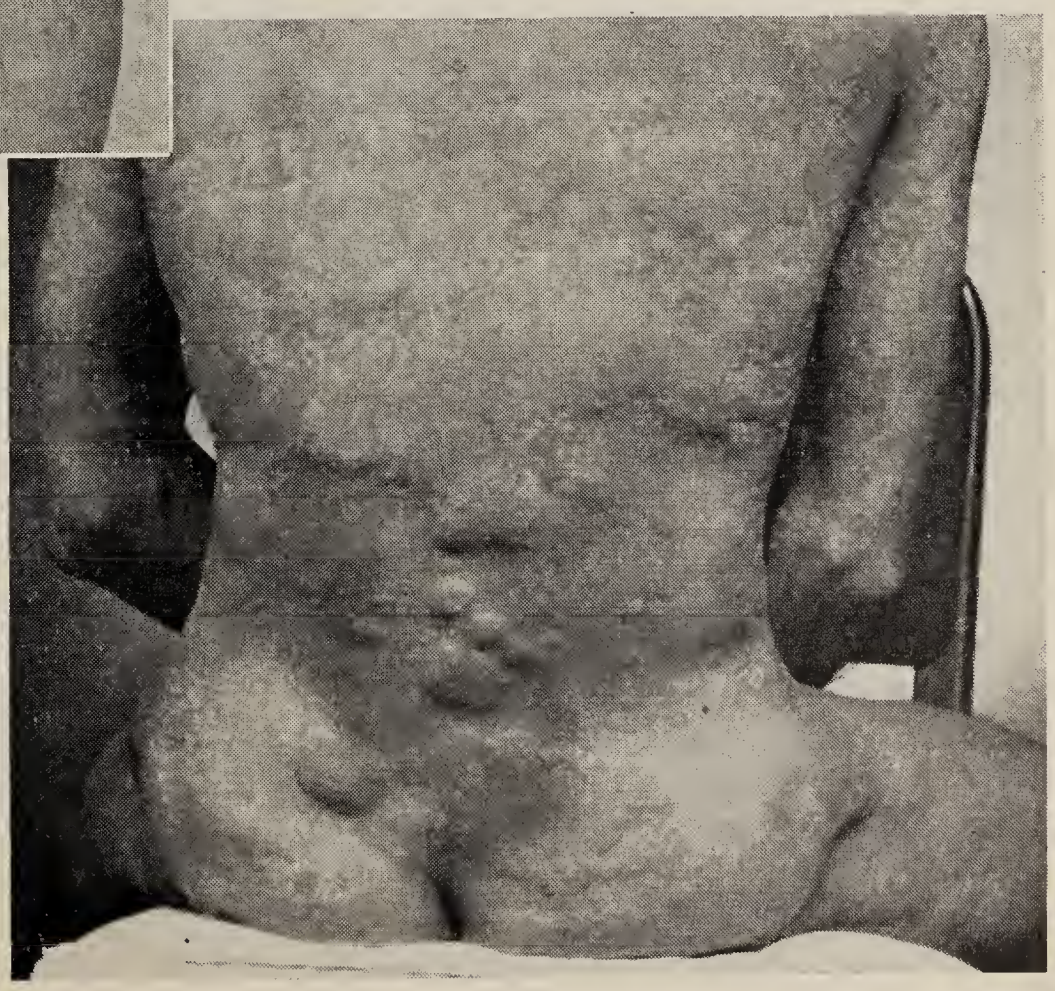

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FIGURE 6. Treatment for an upper respiratory infection was given a few hours before this picture was taken. What has happened? What is the treatment?

INVOLUNTARY MOVEMENTS AND EXTRAPYRAMIDAL LESIONS

P. M. G. GRANT, 5T8

Introduction

MOST movements are, to some extent, involuntary. In us, as in the decorticate cat, such activities as running, scratching, and turning the head toward a mouse can be performed reflexly, with little or no conscious supervision. In the athetotic, they perform themselves relentlessly, uninhibited by higher centres. The patterns for a number of such gross sequences of movement are present in the spinal cord. How are they controlled? How is control lost?

Anatomy and Physiology

Three systems regulate movement. The first, the pyramidal system, consists of upper and lower motor neurons. The cell bodies of the upper motor neurons are located in the motor cortex (area 4) in the precentral gyrus. Fibres descend through the internal capsules of the lentiform nuclei, and synapse with the anterior horn cells in the spinal cord. The upper motor neuron is not capable of discharging the anterior horn cell singlehanded. Rather, it increases its sensitivity to impulses from other sources.

There are two extrapyramidal tracts, whose actions are opposed. The *augmentor* system originates in the motor (4) and premotor (6) areas, synapses in the caudate nucleus and putamen (neostriatum), subthalamus, upper reticular substance, and the vestibular nucleus. Fibres descend in the vestibulo-spinal and upper reticulo-spinal tracts. Its action is to augment the response of motor horn cells to stimuli from other sources such as the otoliths, the stretch reflexes, and the pyramidal tract.

The *suppressor* system arises from narrow strips of the cortex, areas 2S, 4S, 8S, and 19S, and probably also from area 6. All these come under control of area 24. Some of the fibres descend through the internal capsule with the pyramidal tract, while others pass to the globus pallidus, substantia nigra, red nucleus and lower reticular substance. Suppressor fibres descend in the rubrospinal and lower reticulo-spinal tracts, to synapse with anterior horn cells.

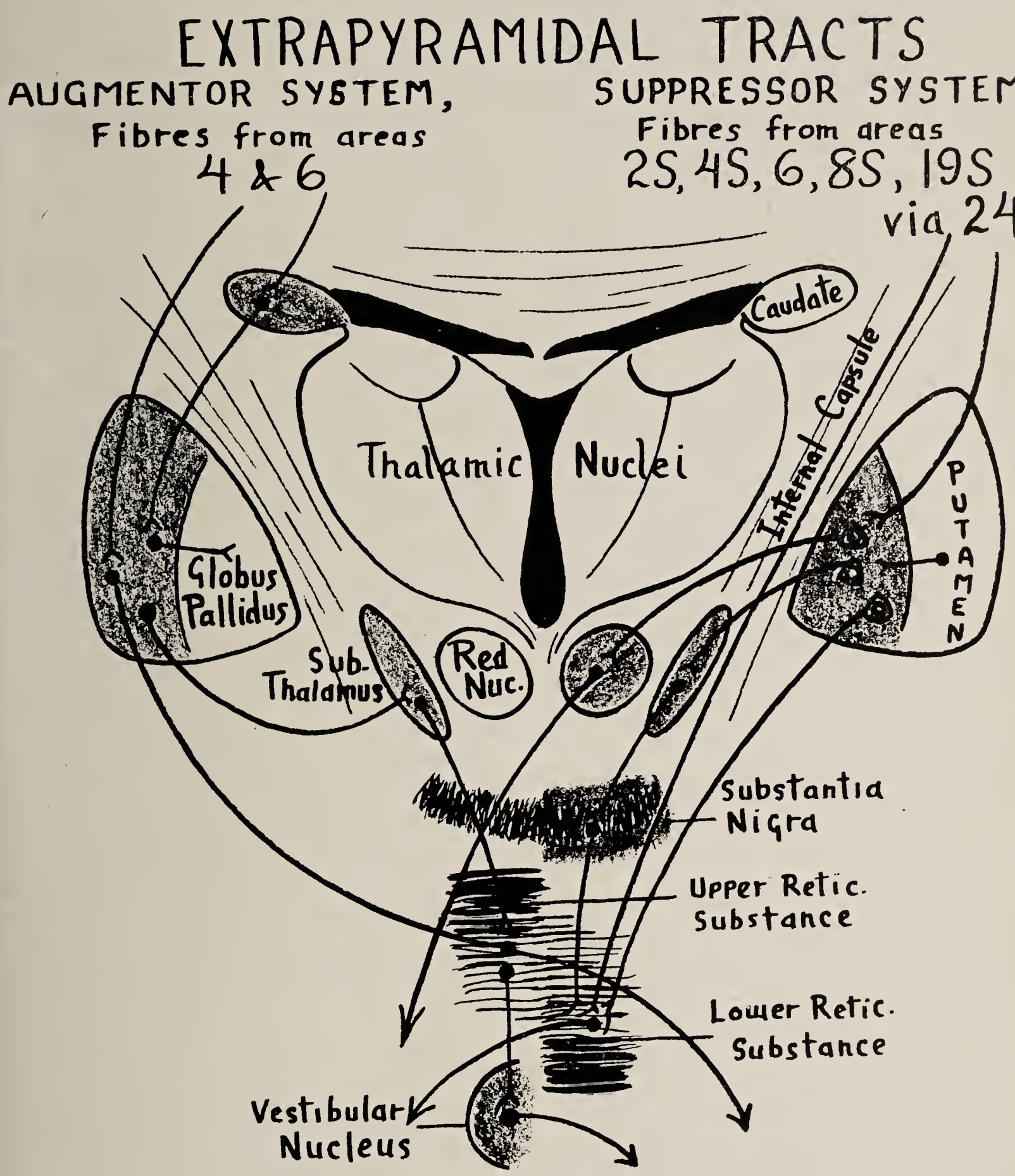
The release of spinal patterns of movement is a suppressor function. Augmentor action produces increased muscle tonus and resistance to movement, both active and passive. For this reason, "augmentor" is a less misleading term than "facilitator". "Suppressor" is misleading too; in regard to its effect on involuntary movements, "releasor" might be as good. Different extrapyramidal syndromes correspond to different combinations of damage to the three regulating systems.

Parkinsonism

Pure suppressor damage is seen in post-encephalitic Parkinsonism, where lesions may be limited to the substantia nigra. In this condition there is marked rigidity, but little tremor. The globus pallidus contains not only large suppressor cells but also some smaller cells from the augmentor system, which share in the damage.

Rigidity results from augmentor predominance, which increases the tonus of all muscles, but initiates no movements. As the pyramidal tract is unaffected, voluntary movement is present, although impeded by augmentor resistance.

Tremor is related to augmentor damage and varies inversely to rigidity. The


EXTRAPYRAMIDAL TRACTS
AUGMENTOR SYSTEM,
Fibres from areas
4 & 6
SUPPRESSOR SYSTEM,
Fibres from areas
2S, 4S, 6, 8S, 19S
via 24
Caudate
Internal Capsule
Thalamic Nuclei
PUTAMEN
Globus Pallidus
Sub-Thalamus
Red Nuc.
Substantia Nigra
Upper Retic. Substance
Lower Retic. Substance
Vestibular Nucleus

pattern of tremor is not localized, either in the cerebral cortex or in the cord, and the movements themselves shift from place to place. The phenomenon of feedback may account for tremor. In the healthy organism, every action sets in motion impulses which travel in long reflex arcs to counteract it and bring it to a smooth, complete stop. When the reflex pathways are interrupted, the descending impulse is delayed and arrives a split second too late. The original action overshoots and is brought back with a jerk. This feeds back more impulses, which are delayed, and so on and so on. The differences in tremors depend on the length of the rerouted pathways. In cerebellar lesions the detour is long, and voluntary movements set up tremors which increase in amplitude as each correcting impulse arrives later than the last. In true Parkinsonism, where the descending augmentor impulse is delayed in the basal ganglia, tremor is stable; it neither increases nor decreases.

ETIOLOGY

The Parkinsonism syndrome appears where suppressor centres are involved by any of the following disease processes:

a. Encephalitis lethargica is the usual cause before the age of 40. It is rare. There is destruction of the pigment-bearing cells in the substantia nigra, with lymphocytic infiltration, perivascular cuffing, and glial proliferation. Much rigidity is present but little tremor.

b. The classical Parkinson's disease, or paralysis agitans, is a primary degeneration of unknown cause. It occurs between the ages of 50 and 60. There are degenerative changes in the cells of the basal ganglia, predominantly the large cells of the globus pallidus. Tremor is marked.

c. Arteriosclerotic disease may affect the basal ganglia, producing a Parkinsonian picture.

d. Wilson's disease (hepatolenticular degeneration), a disorder of copper metabolism, destroys the lentiform nuclei. A Parkinsonian syndrome may result.

e. Rare causes include neurosyphilis, trauma and tuberculosis.

CLINICAL FEATURES

The earliest change is decreased mobility of all muscle groups. The face is "frozen" and changes of expression are slow. The eyes are wide open and staring. The face is smooth. The body and limbs are held slightly flexed. All movements are slow, but not weakened. Speech is slow, monotonous and slurred. Handwriting becomes smaller (micrographia). The gait is shuffling (marche au petit pas) and, once started, walking is hard to stop. Concentrated effort may succeed, for short periods, in normal speech and movement. Rigidity of the muscles is of the "lead pipe" or "cog-wheel" type.

Tremor may begin in one upper limb, spreading in months or years to other limbs. It is stable, coarse, and remarkably constant in rate, usually from 6 to 8 per second. It diminishes on effort, and disappears during sleep. The characteristic tremor is a pill rolling movement, the thumb oscillating upon the first two fingers.

PROGNOSIS

The degeneration is slowly progressive over a period of years.

Choreo-Athetoid Movements

How nice it would be to be able to say that a simple excess of augmentor over suppressor damage, by leaving a relative excess of suppression, freed the spinal

centres to produce involuntary movements unimpeded. This would explain, not only the primitive movements of chorea and athetosis, but the flaccidity and hyperreflexia as well. It would even be consistent with the characteristic lesion of athetosis, a marble-like degeneration (status marmoratus) of the neostriatum. Unfortunately, this lesion, by itself, will not produce athetosis. Not until all three motor regulating systems are damaged are the spinal movements released, both from voluntary control and from spasticity. These conditions are met when hemiplegia and neostriatum damage occur together, most commonly in infantile hemiplegia. Athetosis does not supervene until hemiplegia begins to subside. This, together with the fact that a recurrence of hemiplegia ends athetosis, suggest that some pyramidal function is necessary.

Hemiplegia, caused by internal capsular lesions, does not affect the augmentor tracts. It does affect the pyramidal system and a part of the suppressor system. In the presence of normal augmentor function, pyramidal deficit leads to paralysis, and suppressor deficit leads to spasticity. But in the presence of augmentor deficiency, the spared portion of the suppressor system, its two powerful opponents overthrown, gains the ascendancy.

Now, not only is the tonicity of the muscles lowered, but resistance to spinal movements, formerly maintained by the augmentor and pyramidal systems, is greatly weakened. The primitive patterns creep out of the spinal underbrush and take over. The result is not pure spinal movement. Varying degrees of residual augmentor and pyramidal influences produce various modifications.

Of the wide variety of movements possible, some are recognized clinical entities. Some of the more familiar clinical pictures are:

1. Sydenham's Chorea

This is a disease of children, young adults, and pregnant women. It is usually a complication of rheumatic disease.

ETIOLOGY

There is generalized congestion of the brain, involving both the basal ganglia and the cerebral cortex. The rare fatal cases have shown degenerative lesions of the putamen and caudate nucleus. Augmentor damage is predominant, the suppressor system being largely spared.

CLINICAL FEATURES

The disease often occurs in emotionally unstable individuals. Onset is insidious, the disease often being mistaken for clumsiness. The involuntary movements are described as "semi-purposive". The hand may reach out, as if grasping for some object, and then be flung aside. Upper and lower limbs are involved. Facial expressions are exaggerated. Speech and swallowing may be interfered with. Emotion increases involuntary movements. Co-ordination of movements is lost. Muscle tone is subnormal, and reflexes, although hard to elicit, produce a sustained contraction.

DIFFERENTIAL DIAGNOSIS

Athetosis shows slower, more graceful movements. Huntington's Chorea appears in middle age and is associated with dementia. Habit spasm consists of a constantly repeated movement.

PROGNOSIS

Fatal cases are very rare. Spontaneous recovery occurs in six weeks to three months. Repeated attacks are common.

2. Huntington's Chorea

ETIOLOGY

This is one of the few human diseases which is inherited as a Mendelian dom-

inant. Over 1,000 cases in the United States have been traced back to six individuals, including three brothers who settled there in the seventeenth century.

The cortex, particularly that of the frontal lobes, is atrophied. In the corpus striatum, the ganglion cells are atrophied and reduced in number, and there is glial proliferation. Suppressor damage is more marked than in Sydenham's Chorea.

CLINICAL FEATURES

The disease appears in middle age, and is slowly progressive. Mental changes or involuntary movements may appear first. The movements are rapid, violent, and irregular. Associated are motor ataxia and dysarthria. Mental changes are those of gradual deterioration, often with depression and delusions. Suicide is not uncommon.

PROGNOSIS

The disease is usually fatal in 10 to 15 years.

3. Hemiballismus

This is a disease which resembles chorea, limited to one side of the body.

ETIOLOGY

The characteristic lesion is haemorrhage into one subthalamus which contains both augmentor and suppressor elements.

CLINICAL FEATURES

The movements resemble throwing motions. Its name notwithstanding, the disease can occur bilaterally.

PROGNOSIS

This disease is dangerous as the strenuous activity often proves fatal.

4. Athetosis

ETIOLOGY

(i) The condition supervenes on birth injuries which lead to hemiplegia (Little's paralysis).

(ii) A similar condition results from the combination of recovering arteriosclerotic hemiplegia and lenticular damage.

(iii) Athetosis may occur in Wilson's disease.

The lesions are, first, a marble-like degeneration of the lenticular nuclei, and, second, pyramidal damage, as in hemiplegia.

CLINICAL FEATURES

The movements of athetosis are generally slower, more massive, and more writhing and sinuous than those of the choreas. Facial contortions may be limited to one side of the face whereas those in Chorea are most often bilateral. Athetosis may affect one or both sides of the body. The emotions are labile, and laughing and crying are both frequent. Emotion and voluntary effort increase the movements. The movements disappear during sleep.

Movement affects the distal parts of the limb more than the proximal. Flexion and extension occur at the elbow, wrist, and metacarpo-phalangeal joints, but the phalanges tend to remain extended.

PROGNOSIS

The disease is usually not progressive, and remains unchanged throughout life.

5. Choreo-Athetosis

This term is reserved for clinical patterns which share, or fall between the classical pictures of "Chorea" and "Athetosis". As the differences are mainly differences of degree, there is no clear-cut boundary between the two conditions.

6. Dystonia

This is a condition which differs from Athetosis in that the involuntary movements are rotary and twisting.

ETIOLOGY

The disease has been reported following encephalitis lethargica and other degenerative diseases of the basal ganglia. It may also be familial. Degeneration of the lenticular nuclei and subthalamus has been described.

CLINICAL FEATURES

Onset is usually early, occurring in childhood or adolescence. The movements consist of rotation or torsion of segments of the body on their long axes. Tonicity is alternately increased during movement, but subnormal at rest. The picture may be complicated by signs of the Parkinsonian syndrome.

PROGNOSIS

The disease is usually fatal within one to six years, although survival for as long as thirty years has been reported.

ELECTROCONVULSIVE AND INSULIN COMA THERAPY

CAROLE A. BROADHURST, B.A., 5T8

Historical

SHOCK therapy has been one of the few standard forms of treatment of mental illness for the past twenty years. The term "shock therapy" includes insulin coma therapy (ICT) and electroconvulsive therapy (ECT), both of which are to be discussed in this paper.

The use of convulsions for the treatment of mental disorders dates back as far as 1798 when Weickhardt recommended the administration of camphor to induce vertigo and epileptic fits. The treatment was revived in 1933 when von Meduna recommended giving intramuscular injections of 25% camphor in oil to schizophrenic patients. In 1933 Sakel, observing that insulin was effective in reducing withdrawal symptoms accompanying treatment of drug addicts and that these symptoms resembled those seen in hyperactive states of mental disorders, tried insulin therapy in schizophrenics. Finally in 1938 Cerletti and Bini produced therapeutic fits by passing an electric current through two electrodes placed on the forehead of the patient.

Insulin Coma Therapy

Beneficial results with ICT are achieved only in the treatment of schizophrenia. The best effect is obtained in those in whom the disease is of relatively abrupt and recent onset; the highest recovery rates are among patients in their twenties who have had a sudden stormy onset of their illness. The treatment of such patients should begin as soon as the probabilities point to the diagnosis of schizophrenia even though there is some lingering doubt as to the exact nature of the illness. The quality of the personality before the illness developed is an important consideration in the selection of the patient for treatment: a frank, open, socially well adjusted personality will react best.

TECHNIQUE OF ICT

A careful complete psychiatric, physical and neurological examination is carried out before considering a patient for shock therapy. Contraindications to insulin coma therapy include acute or chronic infection which might be acti-

vated by treatment; serious heart, liver or kidney disease; endocrine disorders; and skeletal pathology.

Careful supervision of the patient for 24 hours after treatment is necessary. There are several methods of administration of the insulin, but only one will be described here. In this method the insulin is administered in rapidly increasing doses on successive days. The fasting patient is given small increasing doses of insulin for five days up to a maximum of 25 u. This is to ascertain whether the patient is predisposed to allergic or hypoglycemic reactions. If there is no reaction, the patient is then given 50 u. deep intramuscular insulin, and the dose is doubled each day until a clinical response is observed or until a maximum dosage of 1600–2200 u. has been reached. Thereafter the daily dose is determined by the patient's response.

SIGNS AND SYMPTOMS ACCOMPANYING TREATMENT

The signs and symptoms observed during ICT correspond to the susceptibility of the different parts of the brain to hypoglycemia—a definite sequence of signs being observed in most cases. Five stages of hypoglycemic symptoms can be described, but there is often overlapping of the stages. Before coma ensues, insulin has a sedative effect on the patient, and may temporarily abolish psychotic symptoms. After the injection of insulin, the patient usually shows symptoms of hypoglycemia for an hour or so consisting of weakness, excessive perspiration, hunger, and drowsiness followed by muscular relaxation marking stage I. Presently he becomes unconscious and passes into shock with tremor and loud breathing (stage II). Stage III is marked by deep coma, loss of primitive movements, and decreased sensitivity to external stimuli. In stage IV there is loss of sensitivity, and in stage V one sees all the above symptoms as well as loss of superficial reflexes and depressed deep reflexes.

The depth and duration of coma induced depend upon the experience and opinion of the therapist. Some believe that stage II is sufficient to produce a therapeutic effect while others insist that stage III, IV, or even V is necessary. Fifteen minutes of stage V would be an extreme limit of safety, and few therapists would permit this depth of coma. Most allow a maximum of two hours of coma per day. The dosage also depends on the nature of the psychotic disturbance being treated and the sensitivity of the patient to insulin.

The coma is terminated by giving adequate amounts of glucose either orally by tube feeding or by intramuscular injection. During recovery from coma there is a return of neural function which suggests a recapitulation of phylogenetic development. Reflexes are the first to appear followed by recovery of crude sensation, motor response and finally, the slow return of mental function. The higher centres are more sensitive to hypoglycemia.

The total course of treatment usually consists of about fifty hours of coma, five to six treatments being given per week. The patient is observed for at least one month after treatment because a relapse may occur any time within this period after discontinuance of ICT.

COMPLICATIONS

Risks accompanying ICT are present, but are not great. They include:

1. Prolonged and irreversible coma in which unconsciousness persists in spite of adequate glucose.
2. Respiratory complications due to the aspiration of saliva or a poorly administered gavage.
3. Cardiovascular complications such as

tachycardia, myocardial failure and aortic insufficiency.
4. Convulsions either early or late of which the latter are more dangerous.
5. Allergic reactions either localized at the site of injection or generalized.

RESULTS

In uncomplicated cases improvement begins with moments of normality during the periods of hypoglycemia; the normal intervals gradually lengthen. After the first few comas, wakening from coma leads to an hour or two of a considerably improved state. The patient then sinks back into his previous state, and remains in it until the next treatment. The state of improved lucidity and accessibility allows the psychiatrist to establish a rapport with the patient and to initiate psychotherapy. As treatments continue, the beneficial changes last longer until improvement is maximal. In order to judge the point of maximum benefit a thorough knowledge of the patient's personality is necessary. Mental improvement is usually accompanied by a parallel physical improvement.

There is great variation in the literature as to the success of insulin coma treatment, but most agree that about 13% fully recovered and 54% improved are the average figures obtained. The results of insulin coma therapy with schizophrenia are not nearly as good as those obtained by electroshock with depressed and manic patients, but it does effect a more rapid cure than psychotherapy alone.

Electroconvulsive Therapy

The use of ECT in the form in which it is used today dates from 1938. ECT is most frequently used in the treatment of depressions accompanying involutional melancholia and in manic depressive psychoses. The use of ECT for neuroses is generally disappointing, and for organic brain conditions it is only of limited symptomatic value for management of disturbing symptoms. It is sometimes used as a substitute for ICT in acute schizophrenic reactions especially in those with affective features.

The selection of the patient depends upon the nature of the illness and the condition of the patient. In the case of manic depressives the treatment is not usually started as soon as the diagnosis is made, but rather time is allowed to see if spontaneous recovery will occur since spontaneous recovery, if it does occur, is more likely to be lasting than improvements due to convulsive therapies. But if the patient begins to go downhill or if there is no recovery over a period of weeks, then ECT is started. In contrast to the above, in cases of involutional depressions, the earlier the treatment is begun the better. Spontaneous recovery, if it occurs, is too late to salvage the wreck of the patient's life.

Even though a complete recovery is not always effected with ECT, the patient's misery is often alleviated, and the duration of the illness may be shortened.

TECHNIQUE OF ECT

As with ICT, a complete careful physical, psychiatric and neurological examination is a prerequisite to therapy. Although the contraindications to ECT are few, the pre-treatment examination is necessary so that appropriate measures may be taken to avoid any complications or exacerbations of existing physical disease. Age, hypertension, abnormal ECG, or history of angina pectoris are not in themselves contraindications provided the general health and personality of the patient are well preserved; however, cardiac decompensation, recent fractures, or tuberculosis usually prohibit ECT.

Pre-treatment mild sedation is often used to alleviate the fears of the patient.

Most therapists use intravenous anaesthesia followed by succinylcholine in the treatment, in which case no special restraining devices are necessary. The current is applied through electrodes on the forehead of the patient. He instantly becomes unconscious, and goes into convulsions.

SIGNS AND SYMPTOMS ACCOMPANYING TREATMENT

The convulsion produced is similar in nature to a grand mal seizure with a tonic phase of about ten seconds followed by a clonic phase of longer duration. There is then a phase of muscular relaxation. The patient remains unconscious for about five minutes usually, slowly rousing over the next five to ten minutes; sometimes he falls into a deep sleep which lasts for ten to thirty minutes. The patient will usually be confused for a short period after treatment, and occasionally there may be a post-convulsive excited state. The patient will have no memory of the shock.

The dose depends upon the threshold of the patient—ranging from 70–130 volts for 0.1–0.5 seconds. Treatments are given three times a week usually, and the period for which treatment is continued depends upon the disorder being treated and the response of the patient. Ten treatments may be enough in some depressive disorders, but as many as twenty-five to thirty applications followed by weekly maintenance treatments are occasionally justified. Often patients can be allowed home between treatments provided they are kept under careful supervision for several hours following termination of the convulsion.

COMPLICATIONS

The complications accompanying ECT are not many. Impairment of memory is an almost constant accompaniment of this treatment. It may continue for several weeks following termination of treatment, and may include memory loss of events for a long period prior to treatment, gradually diminishing to involve events only immediately prior to treatment; full return of memory almost always occurs eventually. Fractures and dislocations can be prevented by the use of succinylcholine prior to the shock. A period of apnea which may be disturbingly prolonged sometimes occurs after ECT. Some therapists use artificial respiration routinely after the convulsion as a preventive measure.

RESULTS

In 80% of the depressions of involutional melancholia and manic depressive psychosis, five to ten treatments are followed by full or social recovery. With the paranoid type of involutional psychoses, however, less than 50% of cases are benefited even by the maximum number of convulsions. Senile depressions can usually be relieved; the manic phase of manic depressive psychosis is sometimes alleviated by more frequent treatments. Whether the early schizophrenics should receive ECT or ICT depends upon the opinion of the therapist, and is a very controversial subject. A course of thirty to forty electroconvulsive treatments probably yields the same results as a course of insulin therapy. Generally schizophrenics treated with ECT do not do as well as those treated with ICT. Some psychiatrists prefer to combine insulin and electroshock therapies for treatment of schizophrenia in order to secure a summation of the benefits of each procedure.

Unfortunately there is a high rate of recurrence after shock treatments of either type. In fact the recurrence rate is higher than that of patients treated without shock, but this form of therapy does shorten the period of acute illness and hospitalization more than any other

type of management. The temporary gain may for the first time create a situation that can be consolidated by psychotherapy.

Mechanism of Action of Shock Therapies

The mechanism of action of the beneficial effects of ECT and ICT is not yet understood. Many theories attempting to explain the therapeutic action of shock have been proposed, but none has been entirely satisfactory.

Some investigators suggest that cerebral anoxia is the basis of the mental change. In ICT hypoglycemia results in cerebral anoxia, and in ECT the increased activity of cerebral function which cannot be sustained by the oxygen and glucose coming to the brain in the blood also results in cerebral anoxia.

Other investigators feel that the therapeutic effect is brought about by disturbance of the hypothalamic centres which in some way restores balance to the autonomic and endocrine systems. Whether the chemical changes in the organism and the alteration of endocrine balance produced by the current are a direct result of the electric current, or an indirect effect of the convulsion, or possibly a result of stimulation of the pituitary or other endocrine glands, is still undecided.

Recent Developments in Shock Therapy

Recent investigations indicate that diffuse stimulation of the entire brain with convulsion-producing currents is not always necessary for the attainment of results. Realizing the probability that the electric current may have a direct effect on certain brain areas without reaching convulsive levels, various authors have begun to test and utilize non-convulsive therapy, thereby obviating the hazards of ECT such as skeletal injuries, apnea and circulatory accidents. So far, however, results with diffuse non-convulsive therapy (NCT) do not measure up to those with ECT, particularly in psychotic disorders although some favourable responses have been reported. The most recent investigative efforts have been directed toward stimulation of specific brain areas, at first with convulsive producing currents and more recently with non-convulsive stimulation of the diencephalon. This latter method has given good results, especially in affective disorders and neuroses. It has been particularly beneficial in disorders which have been refractory to ECT such as manic type manic-depressives and paranoid schizophrenics.

The newer drugs tried in the treatment of schizophrenia have not yet proven as effective as ICT. However, psychotherapy and chemotherapy remain as valuable adjuncts to the physical methods of treatment of mental disease. Shock therapy, although its mechanism of action is not yet understood, will probably be a mainstay in the treatment of certain mental disorders for many years to come.

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INCREASED INTRACRANIAL PRESSURE

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Mechanism

THE skull has often been considered as an inexpansible box containing the brain, the cerebrospinal fluid and the blood in its vessels. When the volume of any one of these contents is increased, there must be a compensatory alteration in the volume of the other contents. If the limits of this normal compensatory mechanism are exceeded, the intracranial pressure is increased.

Theoretically, pressure can be raised by a number of factors: (1) increased cerebrospinal fluid production, (2) diminished reabsorption of cerebrospinal fluid, (3) raised venous pressure intracranially, and (4) an increase in the solid contents of the skull, i.e. a space occupying lesion.

The results of a rising pressure will be determined in the first instance by the rapidity of the rise and development of compensatory mechanisms, and secondly by the period over which the pressure is raised. Brief changes in the intracranial pressure will have little symptomatology. It is high pressure maintained over a considerable period of time which will have clinical effects.

One must remember that the child's cranium is an expansile container with six fontanelles which stay open until 12 to 18 months of age and cartilaginous sutures which do not become ossified until about 15 years of age. For these reasons expanding space occupying lesions in children can often reach a fair size before the manifestations of increased intracranial pressure become apparent.

Aetiology

The following classification is not designed to be all inclusive, nor is any order of frequency intended. Using the four mechanisms mentioned previously the following aetiological factors are recognized.

A. Increased production of cerebrospinal fluid

Certain irritative lesions such as ventricular infections are thought to result in the stimulation of the choroid plexuses, thereby increasing production of cerebrospinal fluid. Increased fluid production can also be caused by papilloma of the choroid plexus and certain forms of meningitis.

B. Diminished reabsorption of cerebrospinal fluid

Obstruction of circulation and, less commonly, a defective cerebrospinal fluid absorbing mechanism can cause a diminished reabsorption of the fluid. This may occur in certain infections when the subarachnoid space around the arachnoidal granulations is obliterated as in some forms of meningoencephalitis, be they viral, fungoidal or bacterial. Other causes of diminished reabsorption are thromboses of the venous channels, usually sagittal sinus, lateral sinus, and sometimes other surface venous pathways.

More commonly intracranial tumours that obstruct the circulation of cerebrospinal fluid prevent the ventricular fluid from reaching the absorptive areas. Obstruction to the ventricular system causes dilatation and filling of the ventricles. A high pressure develops in the ventricles, and this is communicated to the subarachnoid space by the increasing size of the ventricles which constitutes

a space occupying lesion in itself. Other forms of obstruction causing the same effect may result from arachnoidal adhesions in the basal cisterns due to inflammation, from herniation of the temporal lobes and brain stem through the tentorial hiatus, or from cerebellar pressure coning into the foramen magnum.

When the cerebrospinal fluid is confined within the ventricular system the term internal hydrocephalus is used. Here the obstruction is situated at the level of the fourth ventricle or above. Where the obstruction lies outside the ventricles, and produces distension of the subarachnoid spaces (and perhaps the ventricles at a late stage) the condition is called external or communicating hydrocephalus.

Diminished reabsorption of cerebrospinal fluid and its accumulation almost always cause venous compression, and consequent cerebral oedema which further aggravates the increased intracranial pressure, and in turn causes further venous compression.

C. RAISED VENOUS PRESSURE

As mentioned above, raised venous pressure occurs when intracranial pressure is elevated by other means, and is nearly always a secondary phenomenon.

D. SPACE OCCUPYING LESIONS

Increased intracranial pressure and space occupying lesions go hand in hand. A mass incorporates all four mechanisms in elevating the pressure, that is, (1) directly by the tumour, (2) cerebral oedema, (3) obstruction to the flow of cerebrospinal fluid, and (4) obstruction of the venous system.

Three broad aetiological agents are recognized in this group—tumours, haematomata and abscesses.

i. *Tumours:* These can be subdivided into the following classification: (a) Neural—neurofibroma, neuroepithelioma; (b) Meningeal—meningioma; (c) Gliomas—astrocytoma, astroblastoma, glioblastoma multiforme, spongioblastoma polare, medulloblastoma, oligodendroglioma, ependymoma, pinealoma; (d) Vascular and perivascular—angioma, angioblastoma, sarcoma, lymphoblastoma; (e) Mixed—epidermoid, dermoid, teratoma; (f) Hypophyseal—craniopharyngioma, the various pituitary adenomas; (g) Metastatic—from lung, breast, skin, gastrointestinal tract and kidney as five important primary sources.

Seventy per cent of adult intracranial tumours are supratentorial, and 70% of childhood intracranial tumours are infratentorial. When a tumour is located above the tentorium, there is a greater possibility of brain displacement. There may also be downward displacement of the brain stem and portions of the temporal lobes with consequent herniation through the tentorial ring and obstruction of the aquaduct. Such a condition is called pressure coning. Pressure cones arise from herniation of dislocated brain tissue into rigid openings in the skull. The tentorial hiatus and the foramen magnum are the commonest sites for this process to occur. Pressure coning is usually due, not to a generalized increased pressure, but to a continuing local rise of pressure caused by a space occupying lesion. Subtentorial tumours tend to cause blocking of the ventricular system, and therefore manifest increased intracranial pressure early.

Nothing will be mentioned regarding the individual types of neoplasms, for to describe the tumours is in itself a comprehensive subject beyond the scope of this article. The symptoms and severity will of course be determined by the degree of malignancy, rate of growth, location, size of the tumour, and age of the patient.

ii. *Haematomata:* Haemorrhage may

be extradural, subdural, subarachnoid, intracerebral, or ventricular, and may be due to trauma or other causes such as arteriosclerosis and congenital vascular anomalies. Extradural and subdural haematomata particularly cause pressure coning and generalized increased pressure. A subdural haematoma becomes encapsulated, and slowly grows in size because of osmotic pressure differences. Intracerebral haemorrhages also become encapsulated, but as a rule they grow smaller in size, and become reabsorbed; therefore, these do not tend to raise the intracranial pressure. Subarachnoid haemorrhage is likely to increase the intracranial pressure only temporarily because the blood mixes freely with the cerebrospinal fluid throughout the spinal subarachnoid space, and leads to no permanent effects.

iii. *Abscesses:* Brain abscesses are produced by a great variety of bacterial organisms as well as by certain pathogenic fungi, yeasts, moulds, protozoa and other parasites. They are now uncommon (0.4% of autopsies at the Mayo Clinic), and are always secondary to an infection elsewhere (except perhaps for a penetrating wound which has healed leaving a brain abscess). Direct spread to the brain is more common than blood stream invasion.

The area of suppuration in the brain tissue undergoes liquefactive necrosis, and the abscess may or may not become encapsulated. The mechanism of production of increased intracranial pressure is the same as that of any other space occupying lesion.

Clinical Picture

In any neurological disorder, symptoms and signs are manifested as positive or negative phenomena. The former arise as a release mechanism or from an excitation of the nervous tissue, while the latter are caused by destruction and subsequent loss of functional control of that portion of the brain affected. It is well to remember these basic facts when dealing with any neurological lesion.

The clinical picture of raised intracranial pressure is due first to the increased pressure itself, and second to the underlying lesion. Individual symptoms and signs of the underlying lesion are variable according to the nature of the process and the anatomical site. It is useful, therefore, to know the clinical manifestations which may be caused by the high intracranial pressure alone.

HEADACHE

Headache is the commonest feature of raised intracranial pressure. There is little evidence, however, to suggest that the pain is the result of the pressure *per se*, since it is possible to raise the intracranial pressure experimentally without discomfort. Traction or pressure on the pain-sensitive structures in the cranial cavity such as major arteries, veins, dural sinuses, and cranial nerves V, IX, X are responsible for the headache. The pain may be situated on one or both sides, and in the anterior or posterior regions of the head. As a rule both the site and the intensity of the headache vary so that its localizing value may be limited, except for posterior pain which is invariably present in posterior fossa lesions. When the pain is continuous and restricted to one site, its localizing value is greatly enhanced, for in about 30% of the patients the headache overlies the space-occupying lesion.

The headache accompanying increased intracranial pressure is usually dull and aching in character, often intermittent and aggravated by those factors which add stress to the pain sensitive structures already under tension. Such stress includes changes in posture, shaking the head, coughing and straining. It is

characteristically more severe in the morning, and diminishes in intensity as the day progresses. Uncommonly, it may wake the patient during the night or in the early morning when the recumbent posture has been held for some time. Usually not so severe as migraine, it may often be relieved by common analgesic preparations or cold packs.

PAPILLOEDEMA

Oedema of the optic nerve head is a valuable and constant sign of increased intracranial pressure. Evidence of papilloedema is revealed by ophthalmoscopic investigation. The swelling of the optic disc is usually bilateral, but is frequently more marked on one side than the other. Blurring of the optic disc margins with distension and tortuosity of the retinal veins is seen, while the arteries remain normal or are smaller in calibre. Haemorrhages are usually present on or near the swollen disc, and are usually limited to the region around the disc, the surrounding retina appearing normal. From opthalmoscopic examination alone one cannot distinguish between the various causes of increased intracranial pressure, and it does not follow that the lesion is of necessity on the side of the greater swelling.

The papilloedema usually results in an enlargement of the blind spot. Persistent papilloedema results in secondary optic atrophy with a permanent decrease in visual acuity. A tumour may directly compress one optic nerve causing primary optic atrophy, and at the same time the increased intracranial pressure produced by the tumour causes papilloedema of the other eye (Foster-Kennedy syndrome).

In its early stages, papilloedema causes no symptoms, but in time there may be transient attacks of blurred vision, interpreted by some patients as blackouts. Later when secondary optic atrophy ensues, the patient will complain of failing vision which may progress to complete blindness over a period of a few weeks or months.

VOMITING

Vomiting is not correlated with the type or location of the underlying lesion, but when it occurs there is usually marked increased intracranial pressure. Like headache, it is most frequent in the early morning, is not related to meals, and sometimes is projectile and not preceded by nausea. It is often initiated by those actions which raise the intracranial pressure, i.e. rising quickly in the morning, stooping, straining, or coughing. In general, vomiting is considerably more frequent in posterior fossa lesions than those elsewhere, and it is thought that the vomiting centre is irritated due to compression of the medulla.

PERSONALITY CHANGES

About 10% of patients with increased intracranial pressure due to brain tumour display some readily recognizable evidence of mental changes consisting of easy fatiguability, listlessness, and a tendency to become withdrawn. There may be a slowing of the reaction time, inattentiveness, indifference, and a loss of spontaneous activity and resourcefulness. When the intracranial pressure is markedly elevated, yawning, mental clouding, and stupor can occur. In children, moodiness and irritability may develop. Some children become disobedient, lose interest and may prefer to lie down rather than play or eat.

HYDROCEPHALUS

An enlarged head is a very important sign of increased intracranial pressure in an infant or child. The sutures separate, the fontanelles are tense and bulging, and the thin skull bones balloon

under the pressure. A "cracked pot" sound on digital percussion of such a skull can be elicited (Macewen's sign). The superficial scalp veins are often dilated because the pressure inside has forced blood out through the emissary veins.

CONVULSIONS

Convulsions occur in 30% of cases with brain tumour, and even when the attacks are focal in character they are not necessarily related to the site of the lesion responsible for the raised pressure. Seizures which are persistently focal in character have a higher localizing value than focal seizures which are inconstant and occurring late in the disease. Generalized fits are commonest, but they obviously have no localizing value except that they favour the lesion being supratentorial.

VITAL SIGNS

As the intracranial pressure increases, the pulse rate may progressively decrease. The more rapidly the pressure is increased, the greater is the tendency to bradycardia. A rise in intracranial pressure may be accompanied by an increase in blood pressure and a slowing of the respiratory rate, possibly even Cheyne-Stokes respiration. Hiccoughing and cardiac irregularities have also been observed. These vital signs indicate that damage to the brain stem is occurring.

FALSE LOCALIZING SIGNS

False localizing signs arise from involvement of structures far removed from the underlying lesion, and may be produced by damage to the brain tissues from oedema or by pressure coning resulting in compression of structures distal to the lesion.

There are several types of tentorial herniations, the most frequent being hippocampal gyrus impaction leading to oculomotor nerve involvement. The signs and symptoms associated with tentorial pressure coning vary with the type of herniation. When the brain stem is affected, the vital signs mentioned previously will appear. Others include paresis on the same side of a supratentorial tumour due to compression of the contralateral cerebral peduncle, decerebrate rigidity, severe lateralized headache, and temporal lobe phenomena such as uncinate hallucinations and sleep disturbances.

Two other forms of pressure coning, medullary and cerebellar, may give rise to false localizing signs. Headache, neck rigidity, and the vital signs occur with medullary pressure coning. Disturbance of posterior column function (position and vibration senses) may be noted, and can be attributed to pressure from herniated cerebellar tonsils.

Various cranial nerve disturbances occur in conjunction with oedema or herniation. Visual disturbances due to optic and oculomotor nerve palsies are the most frequent findings. The VI cranial nerve is implicated most commonly because of its long intracranial course and consequent susceptibility to downward dislocation with the brain stem. The VII nerve is much less commonly affected in the same manner. Anosmia occasionally occurs with subtentorial tumours due to compression of the olfactory nerve secondary to severe internal hydrocephalus. Tinnitus, vertigo, and a sense of instability, especially when the head is moved, are common symptoms of subtentorial tumours. This vestibular involvement is thought to result from angulation and oedema of the brain stem affecting the vestibular nuclei.

Radiography

The roentgenographic signs of increased intracranial pressure may be divided into two groups: the adult group

(12–14 years and over), and the younger group (under 12–14 years).

IN ADULTS

Demineralization of the sella is reliable evidence of increased intracranial pressure. It is difficult to establish the time necessary for this decalcification to occur, but it probably requires from six weeks to four months depending on the severity of the increased pressure. The parts affected are the dorsum sellae, the posterior clinoid processes, and rarely the anterior clinoids. Demineralization begins posteriorly on the dorsum sellae, and with increasing rise of pressure, it proceeds forward to include the floor of the sella. With more severe pressure of long duration, the posterior clinoids become decalcified. Erosion of the clinoids and flattening of the sella are likely to occur with ventricular distension and pressure from the floor of the distended third ventricle.

Increased digital markings ("pounded brass" or "beaten silver" appearance), an infrequent sign, is said to be due to erosion of the inner table of the skull by the convolutions of the brain.

IN CHILDREN

Separation of the sutures is the most common clinical and radiological sign of elevated pressure in this age group. The coronal, lambdoidal, and sagittal sutures are involved most frequently, and the coronal is probably the most often widened.

Demineralization of the sella is less frequent in children because the pressure is relieved primarily by the separation of the sutures. If sellar changes exist, they are the same as those occurring in the adult. In both age groups, and more particularly in children, when increased intracranial pressure has been present for long periods of time, the sella may become enlarged and simulate an intrasellar tumour.

Digital markings in children should be considered as normal regardless of their appearance if there is no separation of the sutures.

Treatment

The only effective treatment is discovery and removal of the underlying cause. Further radiological investigations are required to determine the nature of the lesion. Pneumoencephalography, which consists of replacing cerebrospinal fluid with air via a lumbar puncture, outlines the ventricular system, which may be enlarged, displaced, or deformed. If raised intracranial pressure has been definitely established or is strongly suspected, pneumoencephalography is a dangerous procedure, and preference is given to ventriculography. Here air is introduced directly into the ventricles through a burr hole in the skull. On plain X-ray the presence of a tumour may displace normally calcified structures such as the pineal gland and the glomi of the choroid plexuses. Arteriography, which outlines the cerebral blood vessels by injection of a radio-opaque dye into the carotid or vertebral arteries, is of great value in the diagnosis of intracerebral disease. This procedure may reveal a shift of vasculature due to a space-occupying lesion, or an abnormally high blood supply to an area of malignancy. Electroencephalography will help to discover and localize a space-occupying lesion.

While the nature of the lesion is being investigated, urgent relief of intracranial pressure may be required. The intravenous injection of a strongly hypertonic glucose solution or a retention enema of magnesium sulphate (200 cc. of a 25% solution) are of very limited value because only temporary relief is obtained, and there is an accompanying disturbance of electrolyte balance in the other body fluids. In most cases surgery plays the

important role in the relief of pressure and in the treatment of the underlying lesion. With malignant tumours the effects of surgical removal of fluid or tumour are short-lived, and the pressure rises to its former level or even higher; but with relatively benign lesions such as meningioma, subdural haematoma and some abscesses, permanent cure may be obtained. Relief of raised intracranial pressure by lumbar puncture or its use for diagnostic purposes when raised pressure is present may precipitate impaction of the brain stem in the foramen magnum, and hence should be discreetly avoided.

Acknowledgement

The author wishes to thank Dr. H. H. Hyland for his valuable counsel in the preparation of this paper.

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PSYCHOSOMATIC ASPECTS OF SCHIZOPHRENIA

S. S. KOLADICH, B.A., 5T8

SCHIZOPHRENIA means, literally, *splitting of the mind*; it may be considered as a psychobiological reaction arising from personal inadequacies and resulting in an inability to adjust to one's environment. Characteristically, there is a progressive withdrawal from personal contact with others, a withdrawal from activities in the environment and regression to a childlike or infantile behaviour pattern. The disorganization or *splitting* of the personality is displayed as an inadequate and inappropriate emotional response to situations, and represents a deterioration of emotional expression. The schizophrenic retreat from reality is a faulty but purposive adaptation in which somatic and mental components concur.

A propensity to attribute a biological identity to schizophrenia is aroused by accounts in the literature where the diagnosis of schizophrenia has been applied to individuals suffering from such conditions as intracranial tumor, chronic hypoglycaemia, epilepsy or hypothyroidism. Many sorts of toxic and infectious processes may present, at the clinically descriptive level, a picture indistinguishable from schizophrenia. Similarly, reactions that are definitely *schizoid* can be produced by drugs such as mescaline, alcohol or morphine. On considering the aetiology of schizophrenia, it may be asked whether the primary disorder is in the brain, or whether we are dealing with a secondary reaction of the brain to a general systemic disorder. In the physical assessment of schizophrenic patients there are objective signs formerly recognized as valuable such as alterations in the

deep reflexes, excessive temperature variations, low basal metabolic rate, disordered gastro-intestinal motor function and polyglandular symptoms.

Research at the physiological-metabolic level shows that hormone factors may be significant in the aetiology or symptomatology of schizophrenia. This is suggested by such characteristics as abnormalities in the oxygen-consumption rate and sugar metabolism, autonomic disturbances, and aberrations of sexual function. However, full blown endocrinopathies are seldom encountered among schizophrenic patients, nor are the victims of recognized glandular disorders particularly prone to schizophrenia. Recently, the concepts of the significance of the inter-relation of endocrinology and psychiatry have undergone fundamental changes. A factor instrumental in bringing about this change was the discovery that the activity of the pituitary gland is related to the functions of the hypothalamus, and thus an obvious neuro-endocrine interacting system was established. Since emotional or other stresses can exert their influence via this mechanism, and thus produce changes in the peripheral ductless glands, there is the effect of *feed-back* to be considered; and so, a vicious cycle can be initiated. In this way, a further deterioration in the mental make-up of a suitable patient may occur. It follows then, that the concern is not with the action of one hormone producing a specific reaction, but that the feed-back will produce changes in other peripheral glands through the effect on the pituitary and hypothalamus, and obviously, mental stress may thus influence not only one, but several of the ductless glands.

Characteristically, in schizophrenia, there is a deficient reaction of the sympathetic division of the autonomic nervous system at the hypothalamic level. The weakened sympathetic and somatic "downward discharge" is expressed in a low blood pressure, depressed circulatory adjustment reactions, and decreased muscle tone, whereas the failure of the hypothalamus to regulate adequately hypophyseal secretions leads to endocrine disturbances. The reduced reactivity of the hypothalamus to cortical stimulation further contributes to defects in homeostasis. The mental changes attending schizophrenia can then be construed as primarily relating to a defective hypothalamic-cortical discharge. Schizophrenic behaviour has been observed in patients as a clinical syndrome associated with cerebral trauma, neoplasm and post-encephalitic involvement of the hypothalamus. Some somatic manifestations of schizophrenia such as postural rigidity and occasional sialorrhoea are similar to changes in encephalitis lethargica where lesions are adjoining the hypothalamus.

A tendency to accumulate colloid has been observed in the thyroid glands of schizophrenic patients representing, functionally, low-grade hypothyroidism. This picture includes all, or a majority of, the following features: scanty urine with downward trends in total solids and total nitrogen but with normal creatinine; subnormal oxygen-consumption rate; downward trend of body temperature, blood pressure and pulse rate; subnormal red blood cell count and elevated lymphocyte count; reduced body weight; decreased vital capacity of the lungs; and sluggish colon-emptying time. Of these abnormalities, some authors regard the triad of low oxygen-consumption rate, secondary anemia and scanty, nitrogen deficient urine as the most significant. In one experiment, five patients with recurrent psychoses exhibiting features seen in periodic catatonia were studied under ward conditions for periods of two to seven years.

During normal periods, all showed a low rate of oxygen utilization (BMR 15–30% below normal). Recurrent psychomotor disturbances in these patients were associated with a rise in the BMR, but were abolished following thyroid hormone administration. Four out of five of these patients have remained well. The hypothesis established was that the underlying defect in these patients was metabolic and that the thyroid hormone in some way facilitated a compensation, returning them to normalcy.

The frequent occurrence of general lassitude, low blood pressure, reduced oxygen assimilation, mild anemia and disturbances of sugar metabolism indicates that adrenal inadequacy may play a significant role in the schizophrenic state. Researchers offer such provocative findings as high sugar curve during stupor, positive galactose tolerance test and diminished physiological response to the administration of cortisone. It seems that the adrenals share in the "schizophrenic-withdrawal" mechanism and most patients show a less than normal morning 17-ketosteroid rise, suggesting that this abnormality is actually one of failure of the cortex to respond to stress. There is retention of fluid, haemodilution, retention of sodium and chloride ions and excretion of potassium ions early and at the height of a schizophrenic attack. Here also is found a substantial increase of androgenic substances in the blood and urine. During recovery and remissions from catatonic episodes there is an increase of sugar-active cortins. However, regarding the disorder itself, the adrenal hormones appear to exert only a secondary, superimposed effect.

Maladjustments in the psychosexual sphere are among the most frequent manifestations of the schizophrenic state. In male patients, the psychosis is characterized by gonadal atrophy and the degree of deterioration correlates with the severity of the psychosis rather than with the age or nutritional state of the patients. Since the development of secondary sex structures is generally rather adequate in schizophrenics, the gonadal effects are of fairly late onset and from the fact that the atrophy is largely confined to the seminiferous tubules, what is primarily at fault is probably a deficiency of gonadotrophic factors from the anterior lobe of the pituitary. Abnormal pituitary gland findings on post-mortem examination of schizophrenics are common, the pituitary glands showing various signs of fibrotic degeneration. X-ray plates of the skulls of schizophrenic patients have detected evidence of hyperpneumatization and sclerosis of the cranial tables indicating the existence of early and prolonged pituitary dysfunction.

One of the most characteristic features of the psychosis appearing at the metabolic level is a deficiency in the uptake of oxygen. However, in the oxygen-consumption rate, as in other physiological processes, the patients are able, episodically, under special stimulation, to rise to normal or approximately normal levels of physiological performance. One indication of the inadequacy of the oxidative mechanisms in the psychosis is a relatively greater accumulation of unoxidized lactic acid in the blood of schizophrenics than in normal subjects when graded exercise is imposed. Further evidence of defective oxygen-assimilation mechanisms is seen in the relationship between the glutathione and lactic acid content of the blood. In tissue respiration, glutathione serves as one of the intermediary bodies whereby the assimilation of oxygen is promoted. Normally the glutathione and lactate levels in the blood, hence in the tissues, vary independently. In schizophrenics, however, when lactate has ac-

cumulated, elevating the titre of that material, the glutathione is found to be low, suggesting that it is being utilized in excess as an adaptive means to facilitate oxygen assimilation.

The schizophrenic possesses an aplastic circulation, a small heart, a low capillary blood flow, and a fairly marked tendency to exhibit hypotension. The total blood volume, when referred to surface area, averages significantly less in schizophrenics than in normal subjects. Among his other handicaps, then, the schizophrenic patient labours under a considerable tendency to circulatory sluggishness. Of still greater significance is the fact that he is much less efficient than normal persons in making adaptive adjustments to local and passing demands upon the circulatory mechanism. These patients frequently exhibit vasomotor-sympathetic disturbances as is evidenced by the appearance of local sweating, edema and cyanosis of the extremities.

Experiments offer evidence that there is an organic change in the vestibular apparatus in schizophrenia. In response to caloric stimulation, both hyperpnoea and alcohol administration caused a decrease in the nystagmic reaction, whereas in normals, an increased nystagmus was noted. Following rotation in a Bárány chair, schizophrenics manifested less than half as much unsteadiness as did normal controls. Altogether then, the evidence is excellent that the schizophrenic is much less than normally reactive in regard to his equilibrium functions. It is difficult to escape the conclusion that the defect here is centrally determined and based upon an organic defect.

One of the most important characteristics of higher species, as some authors have emphasized, is an ability to maintain a steady state—homeostasis—within the individual despite the stresses constantly impinging upon him from the environment, external and internal. In contrast, the schizophrenic exhibits a defective reactivity to such stimulating agents as adrenalin, cortisone, thyroxin, dinitrophenol or foreign protein. This lack of adequate response to such a variety of stimuli might well be regarded as an indication of "schizophrenic withdrawal" at the somatic level. The facts seem to warrant the conclusion that schizophrenics as a group are less than normally reactive to a variety of stimulating agents, and are thus significantly handicapped in their adaptive capacities, leading to inadequate and uneconomical organic responses to changing stimuli. From the point of view of defective homeostasis, then, the psychosis might be regarded as a functional disintegration of the personality due to an inability to meet the demands of maturity with the resources of the immature. It would seem that the prodigality of effort required for organic adaptation leaves the patient with but inadequate energy for successful adaptation in the social field.

It must be considered that the methods of investigation up to the present time have been rather crude, and future improvement in these methods will bring about more sensitive and increasingly accurate investigations. Important data regarding the *aetiopathogenia* of schizophrenia are presently being elicited from researches involving genetical, constitutional, brain localizatory, toxiinfectious and psychopharmacological factors. Among the most striking are the experiments in brain physiology and pathology including parietal syndromes and schizophrenic depersonalization phenomena, the function of diencephalic centres, and the extrapyramidal mechanism of catatonia. Some authors (Kleist) consider a majority of schizophrenias as neurological-heredo-degenerative system dis-

eases such as Friedrich's disease and Huntington's chorea. Studies on toxic or infectious causes of schizophrenia attribute much importance to the excessive or abnormal diamine production due to liver or reticulo-endothelial dysfunction or to gastrointestinal diseases. These cerebrotropic actions of toxic amines show some parallelism with the pathogenesis of phenylpyruvic oligophrenia (also an hereditary recessive disease). Diamines such as bulbocapurine, mescaline and d-lysergic acid evoke schizomimetic effects and strengthen the hypothesis of the existence of specific amino-sensitive cerebral areas (Baruk and Buscaino). Finally, the controversial role of serotonin or enteroamine may be soon uncovered, bringing new insight into the problem. Perhaps the most recent (and therefore the most fashionable) concept of schizophrenia is that it is the result of a *complex aminotoxicosis* (especially in predisposed subjects), particularly by substances with an indole skeleton. Conceivably, this aberration of metabolism has also a viral origin. The first steps towards a biological diagnosis of schizophrenia are just now being made.

Acknowledgement

I wish to thank my wife for the reading of this manuscript and the many helpful suggestions she has given me.

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MYASTHENIA GRAVIS

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Definition

MYASTHENIA gravis is a chronic disease characterized by weakness and easy fatiguability of voluntary muscles.

Etiology

Although all ages are susceptible, myasthenia gravis usually occurs in adult life and the peak incidence is between 20 and 50 years of age. The incidence among females is greater than among males. No true familial tendency has been demonstrated.

The cause of this disease appears to be a functional abnormality at the myoneural junctions of voluntary muscles.

Normally acetylcholine is released at the myoneural junctions when impulses pass across, and the acetylcholine in turn is quickly hydrolysed by cholinesterase. Some abnormality or derangement of this process probably occurs in myasthenia gravis, thereby causing muscle weakness and fatiguability.

The action of curare, quinine and quaternary ammonium compounds produces a state very similar to myasthenia gravis while the anticholinesterase drugs act in the opposite manner by relieving the weakness and muscular fatigue of myasthenics.

Curare is known to act at the myoneural junctions by preventing the normal action of acetylcholine.

Numerous studies concerning the nature of the disorder in myasthenia gravis have been made. Stedman has shown that the blood level of cholinesterase is not increased in myasthenics. There is also no evidence to suggest that there is an increased breakdown or defective formation of acetylcholine.

Wilson and Stoner claim to have demonstrated a toxic factor in the blood of myasthenic patients which interferes with the transmission at the myoneural junctions.

The thymus gland is often found to be enlarged in myasthenia gravis and in 10–20% of cases a thymoma is present. Wilson, Obrist and Wilson have demonstrated in the thymus gland of myasthenics a substance which depresses the muscle response to nerve stimuli.

The exact etiology of the fatiguability and weakness of the muscles in this disease has yet to be elucidated.

Pathology

Russell has described the pathological changes in the muscles as follows:

(i) acute necrosis with inflammatory cellular exudate.
(ii) progressive atrophy with lymphorrhages.
(iii) simple atrophy of single muscle fibres.

Clinical Picture

Clinically this disease is characterized by the development of abnormal fatigue and weakness of voluntary muscles when these muscles are in action. Those most frequently affected are the oculomotor, facial, laryngeal, pharyngeal and respiratory muscles.

The onset is usually gradual with characteristic fluctuations in the severity of the disease apparent from the onset. Occasionally the disease may take the form of a generalized involvement of the skeletal muscles.

Ptosis of one or both eyelids is often the first symptom, and it is usually followed by diplopia as the external

ocular muscles become affected. These symptoms characteristically appear in the evening when the patient is tired, and tend to disappear after a night of rest.

With bulbar involvement the patient may complain of difficulty in swallowing and articulation. The speech assumes a nasal character, and if the patient talks for any length of time the speech becomes indistinct and unintelligible.

Nasal regurgitation of fluids may also occur along with the danger of aspiration of food.

Masseter muscle involvement may result in weak chewing movements, and involvement of the soft palate and the tongue may further aggravate any difficulty in the ingestion of food.

Involvement of the laryngeal muscles, the intercostals and the diaphragm leads to attacks of dyspnoea which gradually become more severe and more frequent. Such attacks may terminate fatally.

When the facial muscles are affected, the patient may be left with a flaccid facial expression, and any attempt at a smile by the patient will only result in a snarl.

The skeletal muscles may be diffusely involved. The most proximal muscles of the pectoral girdle tend to exhibit the weakness and fatigue initially.

Weakness of the neck muscles will tend to cause the head to fall forward, and the patient may find it difficult to walk with the head erect.

Muscle atrophy is not common, but when it occurs the temporal, masseter, cervical and proximal pectoral muscles are the ones which are chiefly affected. Permanent paralysis may occur, the ocular and bulbar muscles being most prone to this development.

Female myasthenics tend to have a decreased fertility, but when pregnancy occurs it terminates with a normal delivery. Remissions and relapses may accompany pregnancy. The offspring of such patients may suffer from mild to severe myasthenia gravis at birth, but complete recovery almost always takes place.

Myasthenic patients are susceptible to intercurrent infections, and in severe cases the myasthenic may become bedridden and helpless.

Prognosis

Individual cases are unpredictable because the disease runs an extremely variable course. Complete remissions of many years duration as well as a rapidly fatal termination of the disease may occur. These extremes are more common in the younger age group.

The onset of the disease is gradual, and the ocular symptoms may persist for many years without any further symptoms. However, even if the muscle involvement is more extensive, frequent and striking remissions may take place, and the condition may remain stationary for years.

In the course of time, in some cases, relapses will tend to occur with greater frequency, and a slow progressive trend toward an increased severity of the disease may become apparent. With progression of the disease, attacks of dyspnoea increase in frequency, and in the final stages the patient may become bedridden and emaciated.

Death often results from bronchopneumonia and cardiac failure.

Diagnosis

The diagnosis of myasthenia gravis does not present much of a problem. The characteristic pattern of weakness and fatiguability may be demonstrated by having the patient perform repetitive movements.

An accurate and reliable diagnostic method consists of the injection of neostigmine 1.5 mgm. and atropine

0.6 mgm. A positive response is indicated by the abolition of weakness and fatigue in half to one hour and the return of symptoms in four to eight hours.

A more satisfactory and more rapid test is the result obtained by the intravenous injection of 0.5 mgm. of neostigmine.

Treatment

1. General Therapy

The activity of patients afflicted with myasthenia gravis should be restricted, and during exacerbations of the disease bed rest is essential.

The management of dysphagia may require intravenous fluids or stomach tube feedings in addition to specific drug therapy.

Respiratory distress may require the additional use of antibiotics, oxygen, bronchial suction and a respirator. Under certain circumstances, a tracheotomy performed under local anaesthesia may be life-saving.

2. Drug Therapy

In the use of the anticholinesterase drugs the optimum dosage for each patient must be individualized. This is determined by increasing the dose until the maximum improvement is obtained.

a. *Neostigmine*

Oral neostigmine is the drug of choice in controlling myasthenia gravis. The preparation is available in 15 mgm. tablets. Most patients can be controlled on oral neostigmine in a dose of 15–40 mgm. every 2–4 hours. Side effects such as abdominal cramps, diarrhoea, nausea, vomiting, excessive salivation and sweating can be prevented by the administration of 0.3–0.6 mgm. of atropine with every other dose of neostigmine.

In emergencies 1 mgm. of neostigmine can be given intravenously or 1–2 mgm. can be given intramuscularly every 1–3 hours.

b. *Pyridostigmine*

This anticholinesterase requires much higher dosages to control a myasthenic. Most patients can be controlled on 120–300 mgm. every 4 hours with the last dose administered at 7 p.m. Pyridostigmine has the same peak effect as neostigmine, but the strength is more evenly distributed between doses. Side effects are controlled by the administration of atropine.

c. *Ambenomium*

This drug is effective in smaller dosages than neostigmine, and it has a longer duration of action. The usual dose is 10–30 mgm. every 4 hours by mouth with the last dose given at 7 p.m.

Except for severe cases anticholinesterase therapy is not required during the night.

d. *Ephedrine and Potassium Salts*

Ephedrine in a dose of 25 mgm. orally three times daily or potassium chloride in a dose of 2 Gm. orally three times daily have been found to be of benefit when used in conjunction with the anticholinesterase therapy.

3. Thymectomy and Irradiation

In 10% of patients afflicted with myasthenia gravis a thymic tumour is present, and up to 70% of patients have been reported to have enlarged thymic glands.

Blalock first reported on the treatment of myasthenia gravis by removing the thymus gland.

Since then studies on the efficacy of thymectomy or irradiation as methods of treatment have brought forth varied results.

Keynes reported that operative removal of the thymus gland in over 200 patients without thymomas gave excellent results in 70% of cases. Preliminary preoperative irradiation improved the results in cases with thymomas.

Schwab and Leland reported that

patients of all ages and both sexes who had thymomas which were demonstrated by either gross or microscopic examination showed no evidence of improvement after undergoing thymectomy.

Another series at Johns Hopkins Hospital showed improvement in 1 out of 4 patients and dramatic remissions in 1 out of 7 patients following thymectomy. Irradiation of the thymic region with 2000 r over 20 days gave similar results.

However, the facts that 25% of myasthenic patients have spontaneous remissions at some time during the course of their disease, and that larger numbers experience various degrees of spontaneous improvement make it difficult to evaluate the results of thymectomy and irradiation.

Patients who were not subjected to the above procedures were not found to run a significantly different course.

In view of the conflicting reports regarding the results of thymectomy and irradiation, the value of these procedures is still questionable. Thymectomy in the younger female patients does, however, seem to be a sound therapeutic measure.

Acknowledgement

The author is grateful to Dr. J. C. Richardson for his helpful criticism in the preparation of this paper.

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ANSWERS TO "ON INSPECTION"

B. M. STEWART, 5T8

Figure 1. The deformed right ankle is an example of a Charcot joint. The arthropathy is characterized by enlargement of the joint, effusion, laxity of ligaments, dislocation and subluxation, fracture and deposition of new bone. The characteristic feature of the lesion is that it is painless.

In this case the patient had tabes dorsalis, the condition in which Charcot joints are most commonly seen; however, they may also appear in patients suffering from syringomyelia and diabetic neuropathy.

Figure 2. There is little doubt that this lesion is a carbuncle, but anthrax may present a primary lesion similar to this picture. It is wise, therefore, to culture the invading organisms. Most carbuncles are of the staphylococcal variety; hence, sensitivities are important.

A massive infection such as this may be the premonition of diabetes mellitus. The wise physician will accordingly check the urine sugar and the glucose tolerance curve. It must be remembered, however, that acute infections such as this can *cause* transient glycosuria.

Conservative treatment seems to be the one of choice. Surgical drainage should be applied only if there is definite

abscess formation. Hot soaks of saturated magnesium sulphate solution every four hours followed by a magnesium sulphate and glycerin dressing are often very effective. Systemic antibiotics should always be employed, preferably broad spectrum antibiotics.

FIGURE 3. This is Trousseau's sign demonstrating low ionized serum calcium levels, and hence, latent tetany.

Nerve excitability is enhanced by low calcium ion concentration in the serum, and its effects are potentiated by ischemia; hence, a nerve-muscle preparation under anoxic and low Ca^{++} conditions will respond to a single stimulus by sustained muscular contraction. The cuff produces ischemia of the forearm musculature. The clinical sign is due to contraction of the forearm and hand muscles, the position depending upon the strength of the various contracting muscle groups.

Hypocalcemia and alkalemia produce clinical tetany. Hypocalcemia occurs in hypoparathyroidism, post-parathyroidectomy states, rickets, osteomalacia, and renal failure with phosphate retention. Alkalemia occurs with excessive ingestion of alkali, in profuse vomiting, and with hyperventilation.

This patient had hypoparathyroidism.

FIGURE 4. Once a child has swallowed, there will be air in his intestinal tract and a gas bubble in the stomach. There is none here; otherwise, the X-ray shows a normal child.

Every time the child was fed he coughed severely, became cyanosed, and regurgitated all the food that he was given. This is the history of one type of tracheo-esophageal fistula with atresia of the esophagus. A characteristic feature is the bringing up of frothy mucus. A catheter passed into the pharynx will confirm the obstruction.

Once the diagnosis is made, the most important factor in management is *do not feed the child.* He should be kept propped up so that the gastric juices will not run into the lungs. Untreated, the child will die in about three weeks, not of inanition, but of aspiration pneumonia or infection of a patch of atelectasis. Antibiotic therapy is essential, therefore, until the child is transferred to a centre of pediatric surgery. Surgical treatment consists of closure of the fistula and anastomotic reconstruction of the esophagus.

FIGURE 5. A caput medusae is illustrated. Although this picture is most commonly associated with cirrhosis, you must not jump to this diagnosis.

The primary pathology is portal hypertension which may be caused by obstruction to the hepatic veins as in cirrhosis, inferior vena cava thrombosis, or malignant involvement of the inferior vena cava. In cirrhosis it is believed that portal hypertension is aggravated by anastomoses between the hepatic arteries with their high pressure and the portal circulation.

A simple test to prove the diagnosis of superficial abdominal varices is that of stripping a vein by hand and observing the direction of flow. Normal flow below the umbilicus is inferiorly; blood in the varicosities of the caput medusae flows superiorly.

FIGURE 6. Following a skin sensitivity test, this patient had been given 1,000,000 units of Penicillin G intramuscularly. The hives and angioneurotic edema seen here are usually only a part of the general anaphylactic reaction of the body. Fortunately for this patient the most feared complications, vasomotor collapse and bronchospasm, did not occur. In some cases, however, Penicillin reactions have been fatal.

A useful classification of the reactions to drugs in general is given in Conn's Current Therapy:

1. the immediate, anaphylactic shocking and sometimes fatal reactions.

2. the classic allergic reactions of asthma, urticaria and nasal symptoms.

3. the delayed serum type reaction with fever, joint pain and hives.

4. skin reactions.

Treatment of anaphylactic effects consists of immediate administration of epinephrine. A tourniquet is applied to the injected extremity in order to reduce further systemic absorption. Epinephrine (1:1000) is given as 0.3 cc. into the site of injection and 0.3 cc. into the opposite side of the body. This is repeated every five minutes depending upon the patient's condition. An injectable antihistaminic such as Benadryl is given as well. Oxygen is given as a supportive measure. In severe cases 20–25 mgm. of ACTH intravenously improves the patient quickly.

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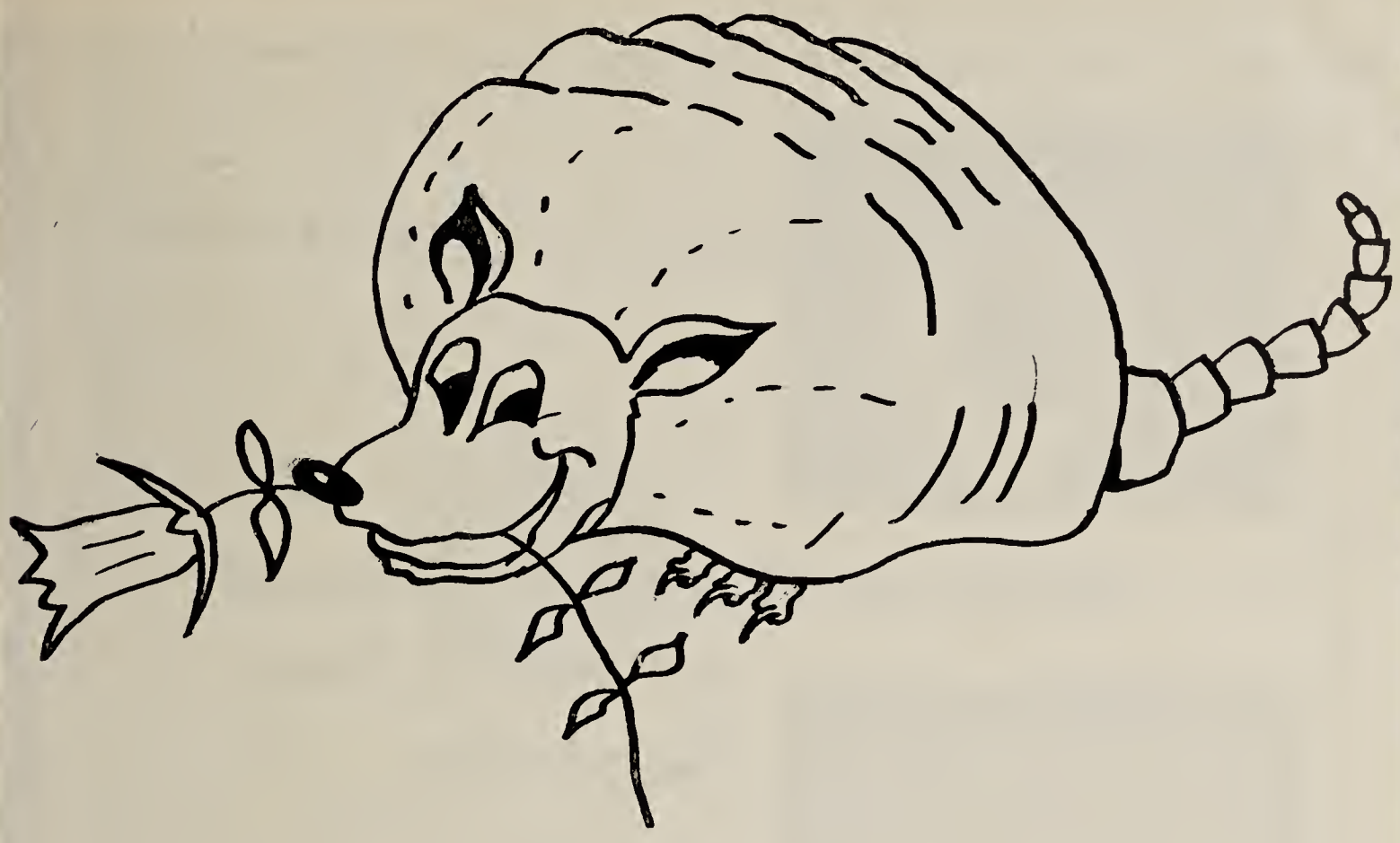

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"...destroyed by 'explosion' within a few seconds..."

VAGISEC*

LIQUID AND JELLY

In a new study of vaginal trichomoniasis in which VAGISEC* liquid and jelly were used, Albert Decker, M.D., reports: "The organism is destroyed by 'explosion' within a few seconds after contacting the [trichomonacide] . . ."[1]

VAGISEC liquid and jelly, used by the Davis technique,† offer a new approach to successful treatment** of vaginal trichomoniasis.[1,4]

High rate of success — Of 65 women considered to have adequate treatment,** 63 were freed of trichomoniasis. "There was immediate relief of symptoms . . ." and no post-treatment recurrences.

Vaginal infections yield promptly — With VAGISEC liquid and jelly, 58 of the 59 re-infection-free patients showed negative smears after three or four weeks of therapy and remained negative through three successive menstrual periods — a criterion of cure. Once extravaginal foci were eliminated, four more cases cleared rapidly. The two failures were in patients whose husbands were infected too.

Explosion unique — Only VAGISEC liquid and jelly explode trichomonads after 15 seconds' contact.[3] A detergent, a chelating agent and a wetting agent, combined in balanced blend, act to weaken the parasites' cell membrane, remove waxes and lipids and denature the protein. Then trichomonads imbibe water, swell and explode.

'Round-the-clock therapy — Physicians use the liquid for office treatments and prescribe it as a home douche, followed by jelly, for 24-hour effective treatment. With this regimen, rate of "cure" averages better than 90 per cent.[4]

Stopping conjugal contagion[1-7] — Many physicians now routinely specify superior RAMSES* prophylactics in writing to prevent conjugal re-infection. RAMSES are transparent, smooth, tissue-thin, yet strong, with "built-in" sensitivity.

Active ingredients in VAGISEC liquid: Polyoxyethylene nonylphenol, Sodium ethylene diamine tetra-acetate, Sodium dioctyl sulfosuccinate. In addition, VAGISEC jelly contains Boric acid, Alcohol 5% by weight.

References: 1. Decker, A.: New York J. Med. 57:2237 (July 1) 1957. 2. McGoogan, L. S.: J. Michigan M. Soc. 55:682 (June) 1956. 3. Davis, C. H. (Ed.): Gynecology and Obstetrics (revision), Hagerstown, W. F. Prior, 1955, vol. 3. 4. Davis, C. H.: West. J. Surg. *63*:53 (Feb.) 1955. 5. Draper, J. W.: Internat. Rec. Med. *168*:563 (Sept.) 1955. 6. Karnaky, K. J.: J.A.M.A. *155*:876 (June 26) 1954. 7. Bernstine, J. B., and Rakoff, A. E.: Vaginal Infections, Infestations, and Discharges, New York, The Blakiston Co., 1953.

*Trade-marks †Pat. app. for

**For a small percentage of women who have an involvement of cervical, vestibular or urethral glands, additional measures are required.[1,3,4]

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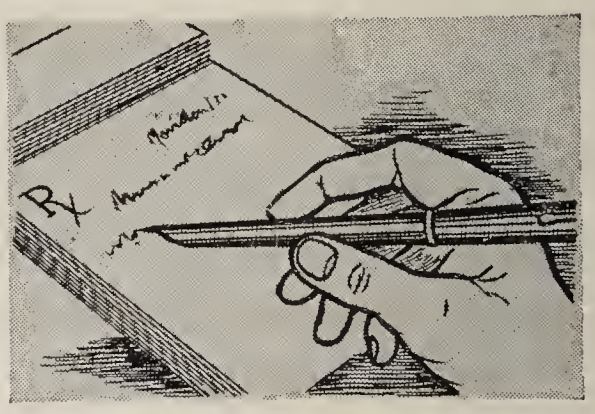

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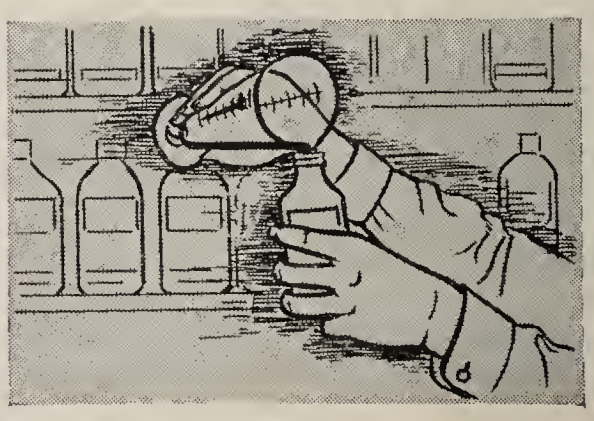

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